

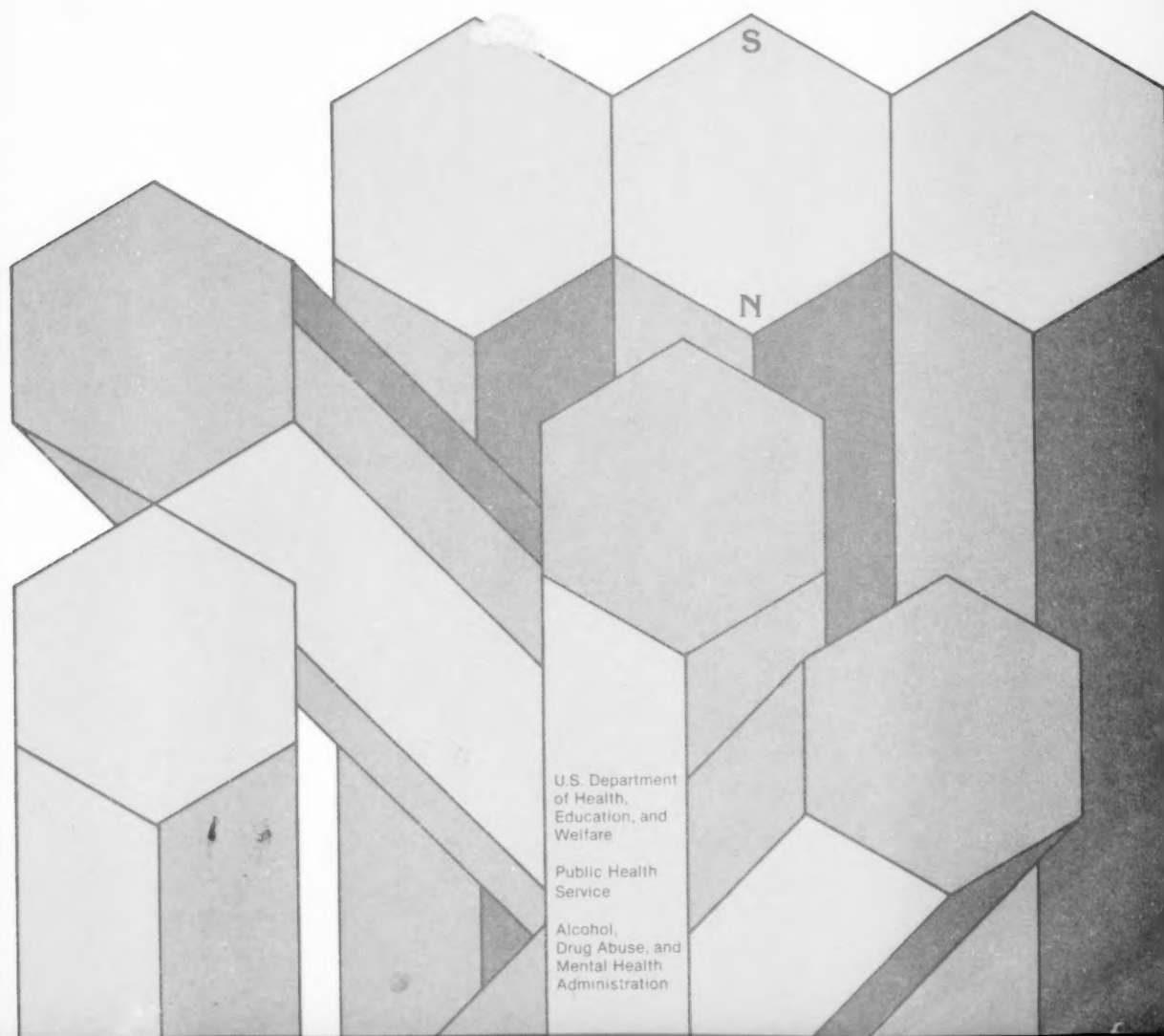
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Carrie Lee Rothgeb, *Editor*

Bette L. Shannon, *Managing Editor*

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ABSTRACTS

PRECLINICAL PSYCOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

001081 Beckett, A. H.; Navas, G. E. Department of Pharmacy, Chelsea College, Manresa Road, London SW3 6LX, England. Some oxidation products of 2-substituted phenothiazines. *Journal of Pharmacy and Pharmacology* (London). 28(Supplement):16P, 1976.

The synthesis, isolation and characterization of some oxidation products of phenothiazine derivatives is discussed. The products were prepared by stirring an acetone solution of the amines with excess manganese dioxide for 30 min in the dark, and then were separated by thin layer chromatography. The oxygen atoms were found to be incorporated into the 3 position, i.e. they were phenothiazones. An intermediate was formed which was a phenothiazine-C-hydroperoxide, which decomposed to give phenothiazines and phenothiazones. The previously reported phenothiazine-N-OH, N-O, and N-OOH compounds are the 3-OH phenothiazines, para-quinoneimino radicals, and 7-OH compounds of phenothiazones. 2 references.

001082 Bruhn, Jan G.; Lundstrom, Jan. Department of Pharmacognosy, Faculty of Pharmacy, Biomedicum, Box 579, S-75123 Uppsala, Sweden. Alkaloids of *Carnegiea gigantea*. Arizonine, a new tetrahydroisoquinoline alkaloid. *Lloydia*. 39(4):197-203, 1976.

The alkaloid composition of the giant cactus or saguaro (*Carnegiea gigantea* Br. and R) was studied in material collected in Arizona and The Netherlands. Chromatographic separation led to the isolation of four tetrahydroisoquinoline alkaloids: carnegine, salsolidine, gigantine and arizonine. The structure of the new natural product, arizonine, was established by spectroscopic data and total synthesis via two independent routes. Salsolidine is reported for the first time in the cacti. Also new to this species are 3-methoxytyramine and 3,4-dimethoxyphenethylamine, which were identified in the alkaloid extract by gas chromatography mass spectrometry. Dopamine was isolated from fresh plant material. 35 references. (Author abstract)

001083 Chatterjee, Asima; Ghosh, A. K.; Chakrabarty, M. Dept. of Pure Chemistry, University College of Science, 92, Acharya Prafulla Chandra Rd., Calcutta 700009, India. Reflexine, a new indole alkaloid of *Rauwolfia reflexa*. *Experientia* (Basel). 32(10):1236, 1976.

Two indolic bases isolated from the leaves of *Rauwolfia reflexa* are characterized. The first base was found to be purpeline through spectral analysis. The second base was found to be reflexine, a new indole alkaloid of this plant and its C-17 epimer. It is noted that reflexine, or 17-epi-seredamine, had not previously been found to occur in natural sources and that its synthesis marks the occurrence of the third epimeric pair of ajmaline like bases currently known.

001084 Dwuma-Badu, D.; Ayim, J. S. K.; Fiagbe, N. Y.; Tackie, A. N.; Knapp, J. E.; Slatkin, D. J.; Schiff, P. L., Jr. Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Science and Technology, Kumasi, Ghana. West Africa Constituents of West African medicinal plants. XV. Dinklacorine, a new biphenyl dibenzodioxin alkaloid from *Tiliacora dinklagei*. *Lloydia*. 39(4):213-217, 1976.

The characterization of *Tiliacora dinklagei* Engl. (Menispermaceae) as a phenolic bisbenzylisoquinoline dibenzodioxin biphenyl alkaloid of structure 1 or 2 is reported and the name dinklacorine is proposed for this new base. Dinklacorine was first isolated in 1974 from extracts of the roots of *Tiliacora dinklagei* Engl. and designated TD-2. The ir, uv and mass spectra of dinklacorine were very similar to those of the dibenzodioxin biphenyl alkaloid tiliacorine. However, the two alkaloids differed in their mp, specific rotation and nmr spectra. Methylation of dinklacorine with diazomethane afforded O-methyltiliacorine, while treatment of dinklacorine with sodium methoxide and methyl iodide gave O-methyltiliacorine dimethiodide. However, prolonged treatment of tiliacorine and dinklacorine with diazoethane afforded different O-ethyl ethers. O-ethyl dinklacorine dimethiodide and O-ethyltiliacorine dimethiodide were different. Acetylation of the two alkaloids with acetic anhydride and pyridine gave O-acetyl esters which were not identical. A consideration of these data and especially the mass spectral fragmentation patterns indicated dinklacorine to be a positional isomer of tiliacorine with the phenolic hydroxy group present in the biphenyl portion of the molecule on the opposite side to tiliacorine. A comparison of the cd spectra of dinklacorine and tiliacorine suggests that they have the same stereochemistry. 18 references. (Author abstract)

001085 Fex, Jorgen; Wenthold, Robert J. Lab. of Neuro-otology, Natl. Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014. Choline acetyltransferase, glutamate decarboxylase and tyrosine hydroxylase in the cochlea and cochlear nucleus of the guinea pig. *Brain Research* (Amsterdam). No.109:575-585, 1976.

Activities of choline acetyltransferase (ChAc), glutamate decarboxylase (GAD) and tyrosine hydroxylase (TH) enzymes catalyzing the synthesis of acetylcholine (ACh), gamma-aminobutyric acid (GABA) and catecholamines, respectively, were measured in the cochlea and cochlear nucleus of the guinea-pig. ChAc activity in the organ of Corti, third turn, was 1270 pmole ACh formed/min/mg protein (ChAc, 1270) and was higher than in turn 4 (ChAc, 543). ChAc activity was higher when the preparation included the inner hair cell region than when not. GAD activity in samples of turn 3 and 4 combined was low, 0.17 nmole GABA formed/min/mg protein (GAD, 0.17). All 3 enzymes were low in the auditory nerve: ChAc, 1.7, GAD, 0.10 and TH, 1.0 pmole DOPA formed/min/mg protein. In the cochlear nucleus, the values were: ChAc, 129, GAD, 1.70 and TH, 2.7. The findings on the distribution of ChAc activity in the organ of Corti fit the hypothesis that the olivocochlear nerve fibers are cholinergic. Because of low GAD in the cochlea, GABA is unlikely to be a transmitter in the organ of Corti. Similarly, it is unlikely that ACh, GABA or a catecholamine is a transmitter between the auditory nerve and the cochlear nucleus. 39 references. (Author abstract)

001086 Gibbs, Irwin S.; Heald, Anthony; Jacobson, Harold; Wadke, Deodatt; Weliky, Irving. Dept. of Pharmacy, Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104. Physical characterization and activity in vivo of polymorphic forms of 7-chloro-5,11-dihydrodibenzoxazepine 5-carboxamide e, a potential tricyclic antidepressant. *Journal of Pharmaceutical Sciences*. 65(9):1380-1385, 1976.

The biological availability in dogs and humans of 7-chloro-5,11-dihydrodibenz(b,e)(1,4)oxazepine-5-carboxamide, a potential antidepressant drug, increased when the compound was administered in capsule formulations as micronized drug coated with 1% sodium lauryl sulfate or as a lyophilate with poloxamer 407. This increase with these two formulations had been predicted by dissolution tests in vitro. The lyophilized combination with poloxamer 407 was more soluble in 0.1N HCl than was the untreated compound. Characterization of the lyophilate by differential thermal analysis, X-ray diffraction, and IR spectroscopy indicated that the increase in solubility was attributable to formation of a polymorphic form. A polymorph of the compound, designated Form B, was prepared. The solubility and dissolution characteristics of two polymorphic forms, A and B, as well as of the lyophilized combination with poloxamer 407, were determined. 15 references. (Author abstract)

001087 Oguakwa, J. U.; Cronlund, A. Department of Chemistry, University of Nigeria, Nsukka, Nigeria **A new alkaloid from *Erythrophleum couminga***. *Lloydia*. 39(4):248, 1976.

The isolation of a new alkaloid from the bark of *Erythrophleum couminga* is reported and the tentative structure of 19-nor-4-dehydrocassaidine was assigned to it. Few alkaloids have been isolated from this species, and the extraction procedure and column chromatographic techniques that were used are briefly described. The sample material was obtained from the Malagasy Republic. 1 reference.

001088 Ott, Jonathan; Guzman, Gaston. Instituto de Investigaciones Biomedicas, UNAM, Apartado Postal 70228, Mexico 20, D.F. **Detection of psilocybin in species of *Psilocybe*, *Panaeolus* and *Psathyrella***. *Lloydia*. 39(4):258-262, 1976.

Analysis of recently described species of *Psilocybe* was conducted and problems concerning reports of the hallucinogenic use of other species of *Psilocybe*, *Panaeolus*, and *Psathyrella* were resolved. Of the two newly described species of *Psilocybe* that were analyzed, only *P. bonetii* contained psilocybin. *P. bolivarii* is the second blueing species of *Psilocybe* reported not to contain psilocybin or psilocin, and possible suggestions are given for the blueing reaction and the failure to detect psilocin. The finding that another species in section *Caerulescentes* (*P. candidipes*) contains psilocybin disproves a previous report that this species is inactive as a hallucinogen. Psilocybin was detected in two species of *Panaeolus*, one of which has been used in the United States as a recreational drug. Mexican specimens of *P. foenicisecii* and *P. sphinctrinus* were devoid of psilocybin and psilocin, consistent with the conception of these species as latently psilocybian. Failure to detect psilocybin in two samples of *Psathyrella sepulchralis* support the contention that these species have been reported as being hallucinogenic because of confusion between this mushroom and *Psilocybe zapotecorum*. 17 references.

001089 Poupaert, J.; Bouche, R. Medical Chemistry Department, Catholic University of Louvain, 4 Van Evenstraat, B-3000 Leuven, Belgium **IR spectroscopic characterization of 2-thiohydantoins and 2-thiobarbiturates**. *Journal of Pharmaceutical Sciences*. 65(8):1258-1260, 1976.

A characterization of 2-thiohydantoins and 2-thiobarbiturates by infrared spectra is proposed. Three characteristic group frequencies, i.e. the thioureide band and the antisymmetric/symmetric stretching modes of NCS bonds, are used. The general characteristic absorption areas are found by comparison with N-phenylthioureas and thioanilides. 13 references. (Author abstract modified)

001090 Rajan, K. S.; Manian, A. A.; Davis, J. M.; Dekirmenjian, H. IIT Research Institute, Chicago, IL 60616 **Metal chelates of L-DOPA for improved replenishment of dopaminergic pools**. *Brain Research (Amsterdam)*. 107(2):317-331, 1976.

A study consisting of physicochemical and animal experiments was undertaken with the objective of developing one or more metal-L-3,4-dihydroxyphenylalanine (L-DOPA) chelate systems for an improved transport of L-DOPA into the brain. Metal chelate systems of in vivo transport experiments were selected which contained the amine bound metal ion in a completely coordinated form. In vivo studies involving the intraperitoneal administration of radiolabelled L-DOPA compounds revealed a 100% to 150% increase in the transport of L-DOPA into the brain by using the cupric chelate and the zinc chelate over that effected by the unchelated compound. The transport effectiveness was also compared with that obtained by using a combination of RO-4-4602, a precerebral DOPA decarboxylase inhibitor, and L-DOPA. 29 references. (Author abstract modified)

001091 Rosengarten, Helene; Meller, Emanuel; Friedhoff, Arnold J. Millhauser Laboratories, Dept. of Psychiatry, New York University School of Medicine, New York, NY **Possible source of error in studies of enzymatic formation of dimethyltryptamine**. *Journal of Psychiatric Research (Oxford)*. 13(1):23-30, 1976.

An assay of an enzyme derived from red blood cells capable of catalyzing the formation of dimethyltryptamine (DMT) from C14-S-adenosylmethionine (C14-SAM), as a methyl donor, and appropriate precursor is described. A hemoglobin free soluble fraction of the red cell was used as an enzyme source. Enzyme protein was incubated with C14-SAM and N-methyltryptamine. Enzyme activity was low but reproducible, and over 80% of extractable radioactivity was authentic DMT product. The product of incubation was identified by chromatography and cocrystallization with authentic DMT carrier. In contrast to the above procedure, if hemoglobin rich undialysed supernate was used as the enzyme source, and C14-SAM in ethanol as the methyl donor, only 11% of the recovered radioactivity migrated with authentic DMT carrier and 89% was confined to the 2-methyltetrahydrobetacarboline (THBC) on TLC. In the hemoglobin rich fraction of the red cell supernate formation of THBC predominates. Formation of C14-formaldehyde from C14-SAM via methanol in the red cell and nonenzymatic condensation with indoleamine substrates followed by formation of THBC is discussed. Proof of THBC formation is presented. 27 references

001092 Ruggieri, George D. New York Aquarium and Osborn Laboratories of Marine Science, New York Zoological Society, Brooklyn, NY 11224 **Drugs from the sea**. *Science*. 194(4264):491-497, 1976.

Marine flora and fauna which contain substances that have antiviral, antimicrobial, tumor inhibitory, anticoagulant, cardioactive, or neurophysiologic properties are discussed. Murexine (urocanylcholine) is present in the hypobranchial body or purple gland of *Murex* trucus and related snails. Murexine manifests intense nicotinic and curariform actions and is used experimentally as a muscle relaxant. Eledoisin, though not present in all species of Octopoda, is a hendecapeptide found in the posterior salivary glands of *Eledone* species. Eledoisin stimulates extravascular smooth muscle and is a potent vasodilator and hypotensive agent in most animals, including man. The action of eledoisin appears to be chiefly peripheral, affecting vascular smooth muscle or postganglionic pathways to blood vessels, or both. Samples of prostaglandins from

specimens of *Plexaura homomalla* possess the active 15S configuration. These fatty acid derived hormones exhibit potent physiological activities in mammals, in that they can stimulate smooth muscle, depress blood pressure, and exert tranquilizing effects on the central nervous system. The last effect is similar to that produced by reserpine and chlorpromazine. 111 references.

001093 Schultes, Richard Evans; Swain, Tony. Botanical Museum, Harvard University, Oxford Street, Cambridge, MA 02138 *De plantis toxicariis e mundo novo tropicale commentationes XIII. Further notes on virolo as an orally administered hallucinogen.* Journal of Psychedelic Drugs. 8(4):317-324, 1976.

The collection and preparation of pellets prepared from the resin of *Virola* bark for oral administration as a hallucinogen used in connection with witchcraft and magic by natives of the area along affluents of the Rio Putumayo in Colombia are described and discussed. 7 references.

001094 Suzuki, Joseph K.; Zirnig, Aija; Manian, Albert A. Regis Chemical Company, 8210 N. Austin Avenue, Morton Grove, IL 60053 *The synthesis of possible di- and tri-hydroxylated chlorpromazine metabolites.* Psychopharmacology Research Branch, DERP, NIMH

The successful syntheses of 3,8-dihydroxychlorpromazine, 3,7,8-trihydroxychlorpromazine and its dioxo derivative, 3,7-dihydroxychlorpromazine, 7,8-dihydroxychlorpromazine and 7,8-dioxochlorpromazine are described along with mass spectral data of these chlorpromazine derivatives. 12 references.

001095 Tateishi, Mitsuru; Shimizu, Hiroto. Dept. of Biochemistry, Nippon Roche Research Center, Kajiwara, Kamakura, Japan *A new metabolic pathway of bromazepam involving attachment of a methylthio group.* Xenobiotica (London). 6(7):431-439, 1976.

The structures of three hitherto unidentified metabolites of bromazepam (all three metabolites contained a methylthio or corresponding oxidized group at the C-6' position of the pyridyl moiety) in the rat were elucidated by four spectrometry methods. Quantitative analysis of the metabolites determined after administration of (14C) bromazepam to rats revealed that the three metabolites together comprised about 6% of the total radioactivity excreted in the 24 hour urine, or about 1% of the dose. Of the three metabolites, methylthio-bromazepam (M7) appears to be formed first from bromazepam. Methylsulphonyl-bromazepam (M4) and methylsulphonyl-bromazepam (M6) may be formed by oxidation of M7 in vivo. 18 references. (Author abstract modified)

001096 Walser, Armin; Zenchoff, Gladys; Fryer, R. Ian. Chemical Research Department, Hoffmann-La Roche, Inc., Nutley, NJ 07110 *Quinazolines and 1,4-benzodiazepines. 75. 7-hydroxyaminobenzodiazepines and derivatives.* Journal of Medicinal Chemistry. 19(12):1378-1381, 1976.

The syntheses of 7-hydroxyaminobenzodiazepines from 7-nitrobenzodiazepines and their subsequent alkylation, acylation and conversion to nitroso and azoxy derivatives are described. The rearrangement of a hydroxyamine to an aminophenol and its oxidation to an aminoquinone are also described. The results of the pharmacological screening for CNS effects are given. 9 references. (Author abstract modified)

001097 Wu, Wu-Nan; Beal, Jack L.; Mitscher, Lester A.; Salman, Kadhim N.; Patil, Popat. College of Pharmacy, Ohio

State University, Columbus, OH 43210 *Alkaloids of thalictrum. XV. Isolation and identification of the hypotensive alkaloids of the root of Thalictrum lucidum.* Lloydia. 39(4):204-212, 1976.

Sixteen alkaloids (homoaromoline, obaberine, O-methylthalicberine, oxyberberine, thalidasine, thaliglucine, thalugosine, obamegine, oxyacanthine, berberine, columbamine, jatrorrhizine, magnoflorine, palmatine, thalifendine, and base A chloride, plus the artifact, 8-trichloromethyl-dihydroberberine) were isolated from the alkaloid fraction of the roots of *Thalictrum lucidum* L. Of these, obamegine, thalugosine, O-methylthalicberine, thaliglucine, obaberine, and homoaromoline were found to possess hypotensive activity in normotensive dogs. Thalidasine, homoaromoline, thalugosine, thaliglucine, obamegine, jatrorrhizine, and columbamine were found to possess antimicrobial activity against *Mycobacterium smegmatis* at a concentration of 100 microgram/ml or less. 20 references. (Author abstract)

001098 Wu, Wu-Nan; Mitscher, Lester A.; Beal, Jack L. College of Pharmacy, Ohio State University, Columbus, OH 43210 *A note on the isolation and identification of the quaternary alkaloids of Phellodendron wilsonii.* Lloydia. 39(4):249-252, 1976.

Isolation and identification of eight alkaloids from the quaternary fraction of *Phellodendron wilsonii*, the cork tree (Huang-peh) of central mountainous Taiwan, are reported. The alkaloids are berberine, columbamine, jatrorrhizine, magnoflorine, palmatine, phellodendrine, thalifendine, and thalphenine. An artifact, 8-trichloromethyl-dihydroberberine, was also isolated from the tertiary fraction. The quaternary alkaloids of this species are very similar to those of *Thalictrum*. This is the first instance of the isolation of thalifendine and thalphenine from the Rutaceae family, as well as isolation of columbamine from a *Phellodendron* species. The bark from *Phellodendron wilsonii* has traditionally been used as an antimicrobial agent. 10 references.

001099 Zirnig, Aija; Suzuki, Joseph K.; Dickson, Donald E.; Laitar, Robert A.; Manian, Albert A. Regis Chemical Company, 8210 N. Austin Avenue, Morton Grove, IL 60053 *The synthesis of possible hydroxylated metabolites of 2-chlorophenothiazine derivatives.* (Unpublished paper). Washington, DC, NIMH, 23 p.

The methods by which 7-hydroxyprochlorperazine, 8-hydroxyprochlorperazine, 7,8-dihydroxyprochlorperazine, 7-hydroxyperphenazine, 8-hydroxyperphenazine, 7,8-dihydroxyperphenazine, 7-hydroxydesmethylprochlorperazine and 7-hydroxychlorpromazine quaternary methyl iodide were synthesized are reported. 14 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

001100 Beyer, Jean Rundlett; Elliott, Henry W. University of California Medical Center, 101 City Drive, South Orange, CA 92668 *A comparative study of the analgesic and respiratory effects of N-allylnorcodeine (nalodeine), naltorphine, codeine and morphine.* Journal of Pharmacology and Experimental Therapeutics. 198(2):330-346, 1976.

In a comparative study, the abdominal constriction test was used to determine analgesia in mice, and the body plethysmograph was used to study respiratory effects of N-allylnorcodeine (nalodeine), naltorphine, naloxone, codeine and morphine, and various agonist antagonist combinations in rats. The analgesia dose response curves for the surrogate pairs,

nalodeine/nalorphine and codeine/morphine, were parallel but had significantly different slopes. Naloxone was a more powerful antagonist of morphine and codeine than of nalorphine and nalodeine. In antagonizing morphine and codeine analgesia, naloxone was the more potent antagonist, nalorphine had a biphasic effect with decreasing activity at higher doses and nalodeine was not an antagonist. Moderate doses of nalorphine depressed minute volume largely by their effect on tidal volume, but high doses stimulated respiratory rate and therefore had less effect on minute volume. Nalodeine depressed minute volume by depressing tidal volume, since all doses initially stimulated and then variably affected respiratory rate. Metabolic rate by either drug short of convulsant doses. Nalodeine depresses the ventilatory response to carbon dioxide and weakly antagonizes the respiratory depressant actions of morphine. 24 references. (Journal abstract)

001101 Bianchi, M.; Butti, A.; Rossi, S.; Barzaghi, F.; Marcarica, V. Roussel Maestretti S.p.A., Reparto Ricerche, Viale Gran Sasso 18, Milan, Italy *Synthesis of 2,1,4,5-benzothiazepines 2,2-dioxides and of 4-keto-2,1,5-benzothiazepines 2,2-dioxides.* European Journal of Medicinal Chemistry (Paris). 11(2):101-106, 1976.

A series of 4-keto-4,5-dihydro-3H-2,1,5-benzothiazepine-2,2-dioxides and 1,2-dihydro-5H-2,1,4,5-benzothiazepine-2,2-dioxides were synthesized and tested for potential CNS depressant activity in mice. Methods used to evaluate muscle relaxant, taming, anticonvulsant, and sedative activity were rotarod, foot shock, antimetrazol, and potentiation of hexobarbital sleeping time. The drugs were also tested in rats for hypoglycemic and diuretic activity. At 200mg/kg orally, none of the compounds showed CNS activity in mice, nor hypoglycemic or diuretic activity in rats. The details of chemical synthesis are given. 9 references.

001102 Bowery, N. G.; Dray, A. Dept. of Pharmacology, St. Thomas's Hospital Medical School, London SE1 7EH, England *Barbiturate reversal of amino acid antagonism produced by convulsant agents.* Nature (London). No. 5583:276-278, 1976.

The possibility that pentobarbitone has a direct action on gamma-aminobutyric acid (GABA) receptors was examined both in rat isolated sympathetic superior cervical ganglia preparations, which possess GABA receptors analogous to those in the mammalian brain, and in vivo on single neurons in the rat brainstem. Findings from Wistar rat ganglia show that pentobarbitone, in amounts which produced no apparent GABA mimetic effects, reversed the actions of bicuculline methochloride (BMC), a selective GABA antagonist. Several suggestions for understanding the mechanism by which barbiturates reverse the effect of BMC or other GABA antagonists are examined, including (a) the ideal that the inhibition of GABA uptake produced by pentobarbitone in vitro could account for the reversal; and (b) the possibility of a difference in agonist and antagonist binding sites. It is also suggested that because barbiturates are useful in the treatment of convulsant poisoning, this action may be related to an effect at sites associated with inhibitory amino acid receptors. 16 references.

001103 Cazin, Jean-Claude; Lesieur, Daniel; Lespagnol, Charles; Cazin, Micheline; Lemaire, Pierre; Brunet, Claude. Laboratoire de Pharmacodynamie, Faculté de Pharmacie, Rue du Professeur Laguesse, F-59045 Lille, France *Chemical and pharmacodynamic study of beta-aminoketones of benzoxazolinonic structure.* Etude chimique et pharmacodynamique

de beta-amino-cetones de structure benzoxazolinonique. European Journal of Medicinal Chemistry (Paris). 11(1):33-42, 1976.

Acetyl-6-methyl-3-benzoxazolinone was used to prepare beta-aminoketones by the Mannich reaction, and the four compounds thus formed were tested for analgesic, antipyretic, antiinflammatory, and neurosedative properties. The chemical structures of the four compounds are given. Acute toxicity was determined in mice for oral, intraperitoneal (i.p.) and intravenous (i.v.) administration. No anticonvulsant activity was observed when tested for protection against pentylenetetrazole or electroshock convulsions. The derivatives were effective in reducing motor activity in mice, counteracting the hyperactivity induced by 3.5mg/kg d-amphetamine i.p., delaying mortality caused by 12.5mg/kg d-amphetamine i.p., potentiating the effects of pentobarbital, and lowering body temperature, with the morpholinic derivative being the most effective. Thus these compounds have a sedative effect, but they are neither major nor minor tranquilizers. The compounds were demonstrated to be antiserotonergic, antihistaminic, and antibradycardic. In addition, the compounds were analgesic and antiinflammatory, and one derivative seemed to moderate experimental nephritis. 38 references.

001104 Cheng, H. C.; Long, J. P.; Van Orden, L. S., III; Cannon, J. G.; O'Donnell, J. P. Department of Pharmacology, Merrell-National Laboratories, Cincinnati, OH 45215 *Dopaminergic activity of some apomorphine analogs.* Research Communications in Chemical Pathology and Pharmacology. 15(1):89-106, 1976.

The dopaminergic activity of 10 apomorphine analogs was studied in rats lesioned unilaterally with 6-hydroxydopamine in the nigro striatal system. Of these 10 compounds, N,N-dimethyl-5,6-dihydroxy-2-aminotetralin (M-7), N-methyl-5,6-dihydroxy-2-aminotetralin (M-8) and N,N-dimethyl-4,5-dihydroxy-2-aminoinidan (DDAI) exhibited potent dopaminergic stimulant activity by causing the rat to turn to the unoperated side. The turning behavior of apomorphine, M-7, DDAI and d-amphetamine were antagonized by haloperidol. M-7 and DDAI also induced pecking in pigeons and their effects were also blocked by haloperidol. It is concluded that M-7, M-8 and DDAI are direct acting central dopaminergic agents. 21 references. (Author abstract)

001105 Costall, B.; Naylor, R. J.; Pinder, R. M. Postgraduate School of Studies in Pharmacology, University of Bradford, West Yorkshire BD7 1DP, England *Characterisation of the mechanisms for hyperactivity induction from the nucleus accumbens by phenylethylamine derivatives.* Psychopharmacology (Berlin). 48(2):225-231, 1976.

A study was carried out to assess the relationships between the molecular structure and the hyperactivity responses to a number of phenylethylamine derivatives after injection into the nucleus accumbens of the rat. 2-Phenylethylamine induced low intensity hyperactivity; the introduction of hydroxyl functions onto the phenyl ring enhanced activity. M-Tyramine, p-tyramine and dopamine caused marked hyperactivity. Methylation of one hydroxyl function reduced activity and 2(3,4-methylenedioxyphenyl) ethylamine was inactive. Agents with substitution of the side-chain (noradrenaline, d-amphetamine and alpha-methyl dopamine) induced marked hyperactivity. Alterations in the chain length markedly reduced activity. A variety of N substituted compounds (adrenaline, epinine, N-ethyl-dopamine, N-isopropyl dopamine and isoprenaline) were potent inducers of hyperactivity. All hyperactivity effects were dose dependent. The hyperactivities induced by dopamine,

noradrenaline and isoprenaline were each inhibited in a dose dependent manner by subsequent injections of fluphenazine into the nucleus accumbens but not by similar injections of saline, solvent, procaine, propranolol or piperoxan. 9 references. (Author abstract modified)

001106 Coupet, Joseph; Szucs, Vera A.; Greenblatt, Eugene N. Central Nervous System Disease Therapy Section, Lederle Laboratories, Division of American Cyanamid, Pearl River, NY 10965 The effects of 2-chloro-11-(4-methyl-1-piperazinyl) dibenzoxazepine (loxapine) and its derivatives on the dopamine-sensitive adenylate cyclase of rat striatal homogenates. *Brain Research* (Amsterdam). 116(1):177-180, 1976.

Tests of the effects of 2-chloro-11-(4-methyl-1-piperazinyl)-dibenz(b,f)(1,4) oxazepine (loxapine) and its derivatives on the dopamine (DA) sensitive adenylate cyclase (AC) rat striatal homogenates were conducted. Fresh striate tissues were incubated in the presence and the absence of DA and loxapine and its derivatives. The addition of DA in the absence of loxapine increased the amount of adenosine-3',5'-cyclic monophosphate (cAMP) formed; in the presence of loxapine the DA response curve was shifted to the right. Two loxapine derivatives were also found to inhibit the DA sensitive AC. It appears that hydroxylation of loxapine at position-7 reinforces the DA receptor blockade property of this agent whereas 8-hydroxylation or demethylation of loxapine abolishes this property. The contention that the AC system may be involved in the DA receptor function is strongly supported and the DA receptor blockade hypothesis as a possible mechanism of action is further substantiated. 9 references.

001107 de Wied, D. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands Behavioral effects of intraventricularly administered vasopressin and vasopressin fragments. *Life Sciences* (Oxford). 19(5):685-690, 1976.

The influence of arginine-8-vasopressin (AVP), the covalent ring, pressinamide (PA), and the C-terminal tripeptide prolyl-arginyl-glycinamide (PAG) administered via one of the lateral ventricles, on the rate of extinction of a pole jumping avoidance response in rats is studied. The covalent ring of AVP, which is involved in memory processes, pressinamide (PA), is highly active following intraventricular administration while the C-terminal part prolyl-arginyl PAG is less active. It is concluded that the covalent ring of vasopressin contains the essential requirements for the behavioral effect of this neurohormone. A second activity site however may be present in the C-terminal portion of the molecule. 29 references. (Author abstract modified)

001108 Eirin, Ana M.; Ravina, Enrique; Montanes, Jose M.; Calleja, Jose M. Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela, Santiago de Compostela, Spain Synthesis and potential neuroleptic activity of new Mannich bases derived from alpha-tetralone and N-aryl-piperazines. *European Journal of Medicinal Chemistry* (Paris). 11(1):29-32, 1976.

Several Mannich bases of tetralone and 6-methoxytetralone with ortho substituted N-phenylpiperazines were synthesized and studied for potential activity as major tranquilizers. The tests used for screening were: variation of spontaneous motor activity, antagonism of drug induced hypermotility, hypothermia, and potentiation of barbiturates. In all tests, male albino mice weighing 18 to 26g were used. The Mannich bases with highest activity were those with methoxy and chloro substituents, and their structural formulae are given. 11 references.

001109 Flammang, Michel; Wermuth, Camille-Georges. Faculte de Pharmacie, Universite Louis Pasteur, 3, rue de l'Argonne, F-67083 Strasbourg, France /2,3-benzodiazepinic systems. Part II. 4-Oxo-3,5-dihydro(4H)2,3-benzodiazepines: synthesis and pharmacologic study./ Systemes benzodiazepiniques-2,3. II. Oxo-4-dihydro-3,5(4H)benzodiazepines-2,3: synthese et etude pharmacologique. *European Journal of Medicinal Chemistry* (Paris). 11(1):83-87, 1976.

Eleven derivatives of 4-oxo-3,5-dihydro(4H)2,3-benzodiazepine were prepared by condensation of o-benzoylphenylacetic acid with hydrazines, and were tested for pharmacologic activity. The chemical structures of the 11 compounds are given. The compounds were tested for their effect on motor activity and emotional manifestations, muscle relaxant effect, and effect on hot plate reaction, all tests being done in mice. Five compounds were observed to be active, and the two most active of these were tested for anticonvulsant effect. Neither of these two compounds protected animals against the convulsant effect of strychnine or pentylenetetrazole. The best of these compounds, isodiazepam, was 1/30 as active as diazepam in antianxiety effect. Methods of synthesis are given. 23 references.

001110 Kretzschmar, R.; Otto, J.; Teschendorf, H. J.; Worstmann, W. Pharmakologische Forschungsabteilung der Nordmark-Werke GmbH, Postfach 44, D-2082 Uetersen/Holstein, Germany /Pharmacological investigations of the sedative and sleep inducing effect of (4'-fluor-4(4-methylpiperidino) butyrophene (melperone)./ Pharmakologische Untersuchungen zur sedativen und schlafanstossenden Wirkung von (4'-Fluor-4(4-methylpiperidino)-butyrophene (Melperon). *Arzneimittel-Forschung* (Aulendorf). 26(6):1073-1076, 1976.

The pharmacological actions of melperone (Eunerpan) were tested and measured in animals. Melperone was found to have less cataleptic and apomorphine antagonizing effect than haloperidol, perphenazine, and chlorpromazine, but more of an effect than thioridazine and clozapine. Melperone was as effective as chlorpromazine and clozapine in inhibiting spontaneous motility, and more effective than thioridazine, but less effective than haloperidol and perphenazine. Melperone significantly reduced night activity, being as potent as thioridazine, but less potent than chlorpromazine. Melperone decreased the waking phase, increased slow-wave sleep, and decreased REM sleep. Similar effects were obtained with chlorpromazine and thioridazine. Melperone diminished muscle tone about as much as thioridazine, but less than chlorpromazine. Melperone caused change in the dominant EEG frequency from theta to delta, and produced an increase in amplitude. It is concluded that the pharmacological spectrum of melperone is similar to that of thioridazine and chlorpromazine, but with a shorter duration of action. 14 references.

001111 Kuhn, F. J.; Stockhaus, K. Abteilung Pharmakologie, C. H. Boehringer Sohn, D-6507 Ingelheim am Rhein, Germany /Test of a few new morphine antagonists in animal experiments./ Prüfung einiger neuer Morphinantagonisten im Tierexperiment. *Arzneimittel-Forschung* (Aulendorf). 26(11):2009-2014, 1976.

The morphine antagonistic properties of 5 new compounds, (-)-N-(furylmethyl)-nordesomorphine HCl monohydrate (Wa 494-Cl), (-)-N(3-furylmethyl)-3-hydroxymorphinan methanesulfonate (Mr 1257 MS), (-)-2(3-furylmethyl)-2'-hydroxy-5,9 alpha-dimethyl-6,7-benzomorphinan methane sulfonate (Mr 1452 MS), 2-(3-furylmethyl) 2'-hydroxy-5,9alpha-diethyl 6,7-benzomorphinan HCl (Mr 1302 MS), and (-)-N-(3-furylmethyl)-

noroxymorphon methanesulfonate (Mr 1767 MS), were studied in mice, cats, and rabbits. The chemical structures of these five compounds are given. Tests were done of analgesic properties (tail pinch, writhing test, hot plate); LD-50 following s.c. injection; morphine antagonist properties (suppression of morphine analgesia in locomotor activity and morphine induced stupor, EEG analysis); and the length of action of morphine antagonism. The results of these tests were compared with tests done with morphine, naloxone, cyclazocine, and nalorphine. The new compounds resembled the profile of naloxone most in that they were pure antagonists of morphine and had no agonist effect. 15 references.

001112 Ohashi, Kyoichi; Tadokoro, Sakutarō. Behavior Research Institute, School of Medicine, Gunma University, Maebashi 371, Japan **Effects of thyroidectomy on amphetamine-induced acceleration of locomotor activity in mice.** *Japanese Journal of Pharmacology* (Kyoto). 26(5):621-624, 1976.

D-amphetamine was administered weekly for 10 weeks to thyroidectomized mice, and effects of thyroidectomy were examined in terms of change in locomotor activity. Locomotor activity was increased with each administration in both thyroidectomized and sham operated control animals, and after the third administration, the activity was significantly enhanced as compared with activity after the first dosing. In the thyroidectomized group, the activity peak after administration tended to be lower and the duration of amphetamine effect tended to be prolonged. 16 references.

001113 Robbins, T. W. Psychological Laboratory, Downing St., Cambridge CB2 3EB, England **Relationship between reward-enhancing and stereotypical effects of psychomotor stimulant drugs.** *Nature* (London). No.1 5581:57-59, 1976.

Two experiments with rats are reported to demonstrate that stimuli with acquired motivational significance (conditioned reinforcers) can be crucial determinants of the selection of responses which form part of a stereotyped pattern of behavior. The first experiment showed that pipradrol injected into rats can facilitate the learning of a novel spatial discrimination task reinforced solely by a stimulus formerly correlated with reward. The second experiment demonstrated that although conditioned reinforced stimuli are important in the selection of the responses which are stimulated by pipradrol, these responses are performed in a perseverative manner, being part of a stereotyped pattern of behavior induced by the drug. Results support the hypothesis that a general action of stimulant drugs is to cause increased repetition of responding, with response selection being dependent in part on environment contingencies. It is felt that this hypothesis can explain the apparent conditioning of stereotypy in amphetamine treated cats, the idiosyncratic nature of the stereotypes of human amphetamine addicts and possibly the apparently meaningless stereotyped activities of certain psychotic states such as autism and schizophrenia. 18 references.

001114 Standridge, Robert T.; Howell, Henry G.; Gyls, Jonas A.; Partyka, Richard A.; Shulgin, Alexander T. Research Division, Bristol Laboratories, Division of Bristol-Myers Company, Syracuse, NY 13201 **Phenylalkylamines with potential psychotherapeutic utility: 1. 2-Amino-1-(2,5-dimethoxy-4-methylphenyl)butane.** *Journal of Medicinal Chemistry*. 19(12):1400-1404, 1976.

The synthesis, resolution, and asymmetric synthesis of 2-amino-1-(2,5-dimethoxy-4-methylphenyl)butane (BL-3912A) is described and its chemical relationship to mescaline is noted. Animal data obtained in rodents are presented indicating that

the compound can be pharmacologically differentiated from dimethoxymethamphetamine (DOM) and amphetamine and that it improves avoidance acquisition in the rat. The compound appears to be free of hallucinogenic side-effects and their accompanying abuse liability and is presently in clinical trial for evaluation as a psychotherapeutic agent. 36 references. (Author abstract modified)

001115 Summy-Long, Joan Y.; Crawford, Isaac L.; Severs, Walter B. Department of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State University, College of Medicine, Hershey, PA 17033 **Effects of subfornical organ extracts on salt-water balance in the rat.** *Brain Research* (Amsterdam). 113(3):499-516, 1976.

The effects of subfornical organ (SFO) extracts on fluid balance in the rat were investigated. Intracerebroventricular (IVT), but not subcutaneous, injection of homogenates of rat SFO produced diuresis, natriuresis, and kaliuresis in the following 8 hour daylight period. During the overnight cycle, consummatory behavior, potassium excretion, and sodium excretion were reduced. Eight hours after IVT injection of SFO media containing the secretory products but no tissue, urine volume was increased. In the overnight cycle, food consumption, sodium excretion, potassium excretion, and urinary sodium ion concentration were reduced. It is suggested that the SFO contains a substance which alters salt/water balance after IVT injection. The substance is water soluble, heat stable, and has a relatively low molecular weight. Release of this substance from the SFO is enhanced by incubation in a potassium enriched medium. 32 references. (Author abstract modified)

001116 Szarvasi, Etienne; Festal, Didier; Grand, Marcel; Depin, Jean-Claude; Chabert, Janine. Societe LIPHA, 115, Avenue Lacassagne, Lyons, France **(Spiro (piperidine-4':6-thiazole) 3,2,-a)pyrimidines: antidepressants and platelet-aggregation inhibitors.** *Spiro-(piperidine-4':6-thiazolo(3,2,-a)pyrimidines): thymoanalept anti-agregants plaquettaires.* *European Journal of Medicinal Chemistry* (Paris). 11(2):115-124, 1976.

A number of derivatives of spiro-(piperidine-4':6-thiazole(3,2,-a)pyrimidine) were prepared and tested for antidepressant properties in vivo and for inhibition of platelet aggregation in vitro. Acute toxicity was determined in Swiss mice po and iv at 48 hr and at 5 days. Antidepressant effect was measured by the antagonism of reserpine induced ptosis at 1 hr, 1 1/2 hr, and 2 hr after injection of 5mg/kg reserpine into Swiss mice. Antidepressant effect was confirmed by inhibition of norepinephrine uptake, potentiation of norepinephrine induced hypertension, and inhibition of tyramine induced hypertension in the anesthetized dog, and increased urinary excretion of normetanephrine with decreased elimination of vanillylmandelic acid in the rat. The most active substances had an n-octyl or a benzyl group on the piperidine moiety and a 2,4-dichloro, or a tetrahydronaphthyl group on the thiazole moiety. The compound with benzyl and 2,4-dichloro substituents had very good therapeutic coefficient (LD-50/ED-50). The methods of synthesis are given. 42 references.

001117 Tobe, Akihiro; Kobayashi, Toshikatsu. Department of Pharmacology, Bioscience Laboratory, Mitsubishi Chemical Industries Co., Ltd., Midori-ku, Yokohama 227, Japan **Pharmacological studies on triazine derivatives v. sedative and neuroleptic actions of 2-amino-4 (4(2-hydroxyethyl)-piperazin-1-yl) 6-trifluoromethyl-s-triazine (TR-10).** *Japanese Journal of Pharmacology* (Kyoto). 26(5):559-570, 1976.

Pharmacological properties of 2-amino-4-(2-hydroxyethyl)-piperazin-1-yl-6-trifluoromethyl-s-triazine (TR-10) were investigated in mice and rats. Chlorpromazine served as a reference compound. TR-10 expressed in general the pharmacological profiles as neuroleptics ascertained by anti-methamphetamine activity, suppression of conditioned avoidance response, taming effects, decrease in exploratory behavior and cataleptogenic activity. Among these effects, anti-methamphetamine action was most potent. Different from chlorpromazine, TR-10 showed a similar pharmacological activity pattern in the intraperitoneal and oral routes of administration. Although the effects relevant to neuroleptics were less potent than chlorpromazine, such were seen with TR-10 at lower doses than those causing muscle relaxation. TR-10 significantly depressed the spontaneous motor activity but showed no anticonvulsant action in mice. Hypothermic action, potentiating effects of hypnotics and alpha-adrenergic blocking action, characteristic to chlorpromazine, were very weak for TR-10. TR-10 also showed low toxicity in mice compared with that of chlorpromazine. In view of the results, TR-10 is considered to be a neuroleptic with moderate sedative effect and weak side-effects. 19 references. (Author abstract)

001118 Wauquier, A.; Niemegeers, C. J. E. Department of Pharmacology, Janssen Pharmaceutica, Research Laboratoria, B-2340 Beerse, Belgium **Bromperidol, a new potent neuroleptic of the butyrophenone series: a comparison of the effects of bromperidol and haloperidol in intracranial self-stimulation.** *Arzneimittel-Forschung (Aulendorf)*. 26(7):1356-1359, 1976.

Bromperidol and haloperidol were compared in an intracranial self-stimulation procedure in adult male Wistar rats weighing 250g. An electrode was stereotactically implanted in the lateral hypothalamic region of the medial forebrain bundle. Rats were trained to press a lever to receive self-stimulation. On Tuesdays, rats received saline s.c. and on Thursdays, one group received bromperidol s.c. and the other group received haloperidol s.c. The drug was administered in a dose of 0.01mg/kg the first week and doubled each week, until a maximum of 0.08mg/kg was reached. Both drugs caused a dose related inhibition of self-stimulation. It is thus concluded that bromperidol is a potent and specific neuroleptic. The chemical formula for bromperidol is given. 9 references.

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

001119 Abdallah, Abdulmunim H.; Roby, Douglas M.; Boeckler, Walter H.; Riley, Charley C. Department of Pharmacology, Dow Lepetit, Midland, MI **Role of dopamine in the anorexigenic effect of DITA; comparison with d-amphetamine.** *European Journal of Pharmacology (Amsterdam)*. 40(1):39-44, 1976.

The role of dopamine in the anorexigenic effect of 3',4'-dichloro-2-(imidazolin-2-yl-thio)-acetophenone hydrobromide (DITA) and its comparison with d-amphetamine was studied in male mice. Pretreatment with methysergide, cyproheptadine, phenoxybenzamine, and propranolol failed to alter the anorexigenic effect of DITA and amphetamine. However, alpha-methyltyrosine and haloperidol significantly antagonized the effect of both DITA and amphetamine. These results seem to indicate that the anorexigenic effects of both DITA and amphetamine are mediated primarily through the dopaminergic system. 31 references. (Author abstract modified)

001120 Agarwal, R. A.; Rastogi, R. B.; Singhal, R. L. Department of Pharmacology, Faculty of Medicine, University of Ot-

tawa, Ottawa, Ontario, Canada **Changes in brain catecholamines and spontaneous locomotor activity in response to thyrotropin releasing hormone.** *Research Communications in Chemical Pathology and Pharmacology*. 15(4):743-752, 1976.

The effects of chronic treatment with thyrotropin releasing hormone (TRH) on the steady state levels of catecholamines, tyrosine hydroxylase (TH), and tyrosine in the brain and on locomotor activity were studied in rats. A dose dependent and time dependent increase in spontaneous locomotor activity occurred which was accompanied by an increase in brain stem TH. Dopamine levels in cerebral cortex were increased but the concentrations of brain stem tyrosine and cerebral cortex norepinephrine were unaltered by TRH. It is suggested that administration of TRH increases the synthesis and perhaps the turnover of brain catecholamines and that this may constitute an underlying mechanism for the antidepressant action of this synthetic hormone. 26 references. (Author abstract modified)

001121 Agosin, M.; Naquira, C.; Paulin, J.; Capdevila, J. Department of Zoology, University of Georgia, Athens, GA 30602 **Cytochrome P-450 and drug metabolisms in *Trypanosoma cruzi*: effects of phenobarbital.** *Science*. 194(4261):195-197, 1976.

The effects of phenobarbital on cytochrome P-450, ribosomes, and drug metabolism by a mixed function oxidase system was studied in *Trypanosoma cruzi*. *T. cruzi* epimastigotes grown in the presence of phenobarbital hydroxylated p-nitroanisole, aminopyrine, or aniline at a rate 2 to 2.5 times that of control cultures. The drugs were slightly toxic, as judged by a moderate decrease in cell mobility. Phenobarbital restored mobility, suggesting that increased metabolism results in protection of the cells. Naphthalene, which was highly toxic (no mobility), was not metabolized by control or phenobarbital treated cells, but some mobility was restored by phenobarbital. Hydroxylation of p-nitroanisole was inhibited by carbon monoxide, SKF 525-A, and metyrapone, all known inhibitors of microsomal monooxygenases, and was dependent on oxygen. Phenobarbital increased the number of ribosomes in the cytoplasm and those associated with the endoplasmic reticulum and nuclear envelope. Concomitantly, the density of the nucleoplasm and mitochondrial matrix increased. Phenobarbital also increased the concentration of cytochrome P-450, the RNA to protein and the lipid to protein ratios. The results suggest that an important factor in the insensitivity of *T. cruzi* (the cause of Chagas' disease) to chemotherapeutic agents may be its ability to metabolize foreign compounds at substantial rates and that this ability is increased by phenobarbital. 25 references.

001122 Alm, Bernt. Department of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg 33, Sweden **Piperidine: effects on locomotor activity and brain monoamine turnover.** *Psychopharmacology (Berlin)*. 50(3):301-304, 1976.

The effects of piperidine hydrochloride (PHCl) on locomotor activity, flexor reflex activity and brain monoamine levels, turnover, and synthesis were studied. Results indicate a sedative action and an increased turnover of noradrenaline (NA), but no effects on 5-hydroxytryptamine (5-HT) or dopamine (DA). Data obtained from flexor reflex experiments suggest that this is not secondary to alpha adrenergic receptor blockade. One explanation might be an increased impulse activity of NA neurons. 37 references. (Author abstract modified)

001123 Altura, Burton M. Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, NY 11203 **Sex and estrogens in protection against circulatory stress**

reactions. *American Journal of Physiology*. 231(3):842-847, 1976.

Wistar rats were studied to determine whether sex and administration of synthetic estrogenic hormones could influence: 1) survival of rats (male and female) through different forms of lethal circulatory trauma; 2) the phagocytic function of the reticuloendothelial system (RES) in rats; and 3) the tone of splanchnic microvessels of rats subjected to lethal forms of circulatory trauma. Data are presented which indicate that inbred females: 1) have a greater ability to clear particulate matter from the bloodstream than do males of the same strain; 2) are significantly more resistant to two different forms of lethal circulatory stress intestinal ischemia and whole body trauma than are males; and 3) exhibit a greater resistance to undergo RES phagocytic depression after both forms of lethal trauma than do males. Estradiol treatment of males, using either acute, massive or multiple, low dose regimens, confers trauma resistance on such animals. Such estradiol-treated male rats exhibit hyperactive RES's. Direct microscopic observation of rat mesenteries indicates that, in the late stages of lethal intestinal ischemia or whole body trauma, the untreated females as well as the estradiol treated males exhibit significantly less dilatation of microscopic capacitance vessels (venules) than do untreated male rats. The data could be used to suggest that estrogenic hormones may play pivotal roles in the amelioration of an organism's reaction to systemic stress; and control of macrophage and peripheral vascular functions. 40 references. (Author abstract modified)

001124 Anderson, David E.; Yingling, John E.; Brady, Joseph V. Johns Hopkins University School of Medicine, Baltimore, MD 21205 Cardiovascular responses to avoidance conditioning in the dog: effects of alpha adrenergic blockade. *Pavlovian Journal of Biological Science*. 11(3):150-161, 1976.

The cardiovascular responses of blood pressure and heart rate patterns observed in dogs during preavoidance and avoidance conditioning in nondrug control sessions were compared with blood pressure and heart rate patterns during preavoidance and avoidance in other sessions during which alpha-adrenergic activity was suppressed by infusion of phenoxybenzamine. Extended training resulted in the emergence of a cardiovascular response pattern during the preavoidance interval characterized by gradual increases in blood pressure together with decreases in heart rate. Elevations in both blood pressure and heart rate were sustained during the avoidance period. During sessions in which alpha-adrenergic activity was suppressed by phenoxybenzamine, absolute levels of blood pressure were found to be lower than during control sessions, but a progressive rise in blood pressure continued to be observed during preavoidance. These results suggest that sustained cardiovascular responses during avoidance periods are associated with activation of the sympathetic nervous system, but that the gradual rise in blood pressure during preavoidance is due to other factors. 40 references. (Author abstract modified)

001125 Angel, Charles; DeLuca, Donald C.; Murphree, Oddis D. Neuropsychiatric Research, Veterans Administration Hospital, North Little Rock, AK Probenecid-induced accumulation of cyclic nucleotides, 5-hydroxyindoleacetic acid, and homovanillic acid in cisternal spinal fluid of genetically nervous dogs. *Biological Psychiatry*. 11(6):743-753, 1976.

Measurements of probenecid induced accumulation of acid metabolites in cisternal cerebrospinal fluid (CSF) were carried out on 40 dogs, 20 each of a genetically nervous strain and of a normal strain of pointers. The nervous strain after about age

3 months displays extreme hypervigilance, timidity, human avoidance, and often shows catatonic like muscle rigidity when in the presence of humans or novel stimuli. Among the compounds measured at from 1.5hr to 6.0hr after probenecid treatment, homovanillic acid (HVA) was similar for the two strains, 5-hydroxyindoleacetic acid (5-HIAA) was lower, but cyclic adenosine-3',5'-monophosphate (cAMP) and cyclic guanosine-3',5'-monophosphate (cGMP) were higher for the nervous strain when compared with behaviorally normal dogs of the same age and sex. Probenecid levels in CSF were similar at all points in time from 1.5 to 6.0hr after its intravenous administration. These findings, coupled with previously observed differences in the two strains, suggest that hyperresponsiveness of the central nervous system (CNS) noradrenergic and cholinergic systems and a hyporesponsiveness of the serotonergic system are related to the genetically expressed aberrant behavior. 32 references. (Author abstract modified)

001126 Anisman, Hymie. Department of Psychology, Carleton University, Ottawa, Ontario K1S 5B6, Canada Effects of scopolamine and d-amphetamine on locomotor activity before and after shock: a diallel analysis in mice. *Psychopharmacology (Berlin)*. 48(2):165-173, 1976.

The effect of shock on locomotor activity was evaluated in three strains of mice (A, DBA/2 and C57BL/6) after treatment with scopolamine and d-amphetamine. The effectiveness of either drug in increasing locomotor activity was strain dependent. Both drugs eliminated behavioral suppression induced by shock, and in A and DBA/2 mice shock augmented the locomotor stimulation induced by d-amphetamine. The behavior of the six F1 hybrids was examined in relation to the parent strains. It was observed that locomotor activity in the F1's could resemble that seen in one parent in the saline condition, but the other parent after treatment with d-amphetamine. Similarly, the F1 behavior in the amphetamine condition was not predictive of the behavior seen after shock plus amphetamine. It is suggested that general activity, locomotor activity after amphetamine treatment, and responsiveness following shock in amphetamine treated mice are mediated by different genetic mechanisms. 31 references. (Author abstract modified)

001127 Arienti, G.; Corazzi, L.; Woelk, H.; Porcellati, G. Department of Biochemistry, Medical School, University of Perugia, C.P. 3, I-06100 Perugia, Italy Biosynthesis of rat brain phosphatidylcholines from intracerebrally injected choline. *Journal of Neurochemistry (Oxford)*. 27(1):203-210, 1976.

The incorporation of radioactive choline into lipid and water soluble compounds of rat brain was determined at very short intervals after its intracerebral injection, in order to elucidate the relative role of different pathways in vivo. The time course of incorporation of choline into brain lipid is biphasic with two flex points at about 20 and 120 s from the injection. The specific radioactivity of different phosphatidylcholines appears to be different at early and later intervals from injection. The suggestion is made that the base exchange pathway for choline incorporation into lipid might be operative in vivo in early periods after administration. 24 references. (Author abstract modified)

001128 Arnaud, M. J. Nestle Products Technical Assistance Co., Research Dept., P.O. Box 88, CH-1814 La Tour-de-Peilz, Switzerland Metabolism of 1,3,7-trimethylxanthine in the rat: new metabolic pathway of caffeine. *Experientia (Basel)*. 32(10):1238-1240, 1976.

The metabolism of 1,3,7-trimethylhydrouic acid, a caffeine derivative, was investigated in male Sprague-Dawley rats. Thin layer chromatography was used to isolate this substance from the urine of rats fed caffeine. The isolated substance was then fed to rats. Results show that ingestion of caffeine gave rise to 1,3,7-trimethylhydrouic acid which was excreted, along with its metabolites, into the urine. Ingestion of 1,3,7-trimethylhydrouic acid resulted only in excretion of this substance. It is concluded that 1,3,7-trimethylhydrouic acid is a final product of caffeine metabolism and that a new metabolic pathway for caffeine must be derived. A suggested model is presented.

001129 Arora, Ramesh C.; Meltzer, Herbert Y. Dept. of Psychiatry, Univ. of Chicago Pritzker School of Medicine, 950 East 59th Street, Chicago, IL 60637 *In vitro* and *in vivo* inhibition of rat liver, brain and muscle monoamine oxidase by chlorpromazine and imipramine. *Research Communications in Chemical Pathology and Pharmacology*. 14(4):755-758, 1976.

Male Sprague-Dawley rats were injected intraperitoneally with chlorpromazine, imipramine, or fluphenazine decanoate in a study of the *in vitro* and *in vivo* inhibition of monoamine oxidase (MAO), specifically of deamination of serotonin (MAO-A) and benzylamine oxidation (MAO-B) in brain, liver, and skeletal muscle. The results indicate that treatment with imipramine, chlorpromazine or fluphenazine decanoate in relatively high doses does not lead to inhibition of skeletal muscle MAO-A. Imipramine, but not chlorpromazine or fluphenazine decanoate, inhibited rat muscle MAO-B *in vivo*. This indicates that treatment with neuroleptic drugs on a chronic basis does not affect skeletal muscle MAO activity in man but the tricyclic antidepressants might. Thus, deamination of MAO activity in muscle of psychotic patients treated with neuroleptic drugs may provide an indication of endogenous MAO activity in that tissue. 21 references.

001130 Atterwill, C. K.; Neal, M. J. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England *The subcellular distribution of 14C-HABA and 3H-dopamine in the retina*. *Journal of Neurochemistry* (Oxford). 27(2):529-537, 1976.

Subcellular distribution of labeled gamma-aminobutyric acid (GABA) and dopamine in rabbit retinae was studied with respect to their functional role in retinal synaptic transmission. Rabbit retinae were homogenized in isotonic sucrose and subjected to differential and density gradient centrifugation. Preliminary electron microscopic examination of some of the fractions indicated that besides subcellular particles usually observed in brain homogenates, the photoreceptor cells gave rise to several characteristic fragments, including outer limbs, aggregations of mitochondria, and photoreceptor terminals. Unlike the synaptosomes formed from conventional type of synapses in the retina, these terminals appeared to sediment mainly in the low speed crude nuclear pellet. Retinae were also incubated with low concentrations of 14C-GABA and/or 3H-dopamine prior to fractionation, and in these instances the pellet was further fractionated on sucrose density gradients. Analysis of radioactivity in fractions showed that labeled GABA was accumulated by osmotically sensitive particles which had the sedimentation characteristics of synaptosomes. The particles accumulating dopamine appeared to belong to a different, slightly lighter population than those accumulating GABA. It is suggested that particles accumulating labeled GABA were synaptosomes because the fractions containing these particles also possessed most of the glutamate decarboxylase activity of the gradient; in contrast GABA transferase

and monoamine oxidase activity was found in the dense fractions of gradients usually associated with mitochondria. When retinae were incubated with a high concentration of labeled GABA a lighter population of particles seemed to accumulate the amino acid than when a low external GABA concentration was used, suggesting that high and low affinity uptake processes for GABA in the retina may have different cellular sites. 48 references. (Author abstract modified)

001131 Avakyan, R. M. Chitinskogo meditsinskogo instituta, Chita, USSR *Effect of striatectomy on the course of pentylenetetrazol convulsions in the rat*. *Vliyanie striatektomii na techeniye korazolovykh sudorog u krysa*. *Byulleten' Eksperimental'noy Biologii i Meditsiny* (Moskva). 81(3):316-319, 1976.

A series of 268 experiments was carried out on 98 nonlinear white rats to study behavior and EEG manifestations of pentylenetetrazol convulsions after destruction of the striatum. There was no significant disturbance in spike wave activity but a sharply inhibited provocation of myoclonia and its conversion to tonicoclonic convulsions occurred. There was also an increase in the threshold, duration, and severity of the seizure. In 50% of the rats, epileptic status develops. Striatectomy eliminates action of catecholaminergic agents (apomorphine, DOPA, haloperidol and chlorpromazine) on thresholds of myoclonic jerks and seizures. The study revealed an important role of the striatum in development of pentylenetetrazol convulsions and in the generalized attack. 4 references.

001132 Avakyan, R. M. Kafedra farmakologii meditsinskogo instituta, Chita, USSR *Role of striatum in the effect of serotonergic agents on corazol convulsions in rats*. *O roli stratum vo vliyani serotoninergicheskikh veshchestv na techeniye korazolovykh sudorog u krysa*. *Byulleten' Eksperimental'noy Biologii i Meditsiny* (Moskva). 82(7):789-792, 1976.

Effect of electrostimulation and excision of the striatum on the capacity of 5-oxytryptophan and para-chlorophenylalanine to modify indices of corazol convulsions was studied in 65 white rats. The effect of serotonergic agents on behavioral and EEG phenomena of corazol convulsions was examined in intact rats, rats whose convulsive state was caused by electrostimulation of the striatum, and those who had undergone striatectomy. The data show that the striatum plays an important role in the action of serotonergic substances on generalized attacks and postconvulsive conditions, but in preattack phenomena the influence of these substances depends on other mechanisms. 6 references.

001133 Ayhan, I. H. Department of Pharmacology, Ankara University Medical School, Sıhhiye-Ankara, Turkey *Potentiation of morphine-induced seizure by 6-hydroxydopamine*. *Archives internationales de Pharmacodynamie et de Therapie* (Ghent). 223(2):282-286, 1976.

The influence of depletion of brain catecholamines by intraventricular injection of 6-hydroxydopamine (6-OHDA) on morphine induced convulsions was investigated in rats. Morphine, in doses up to 100mg/kg did not produce any convulsive pattern in vehicle pretreated rats. Pretreatment with 6-OHDA strongly potentiated the seizure producing activity of morphine and the dose/response curves of the seizure severity shifted to the right. It is suggested that brain catecholamines are involved in the mechanism of morphine induced convulsions. 24 references. (Author abstract modified)

001134 Back, D. J.; Singh, Jagmohan K. G. Department of Pharmacology and Therapeutics, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England *The biliary excretion of*

(3H) lysergic acid diethylamide in Wistar and Gunn rats. *Experientia* (Basel). 32(5):616-617, 1976.

The biliary excretion of labeled lysergic acid diethylamide (3H-LSD) was studied in Wistar and homozygous Gunn rats. In Wistar rats approximately 46% of the given dose was recovered from bile in 2.5 hours, whilst in the homozygous Gunn rat 26% was recovered in the same time period. In both strains the main metabolites were glucuronides. If it is assumed that, due to the absence of endogenous bilirubin glucuronide in the Gunn rat, there is a marked increase in canalicular transfer of a drug/glucuronide conjugate, there would seem to be a significantly depressed rate of formation of glucuronides of LSD or metabolites in this strain. This suggests the direct involvement of bilirubin glucuronyltransferase in the formation of such conjugates in the normal rat. The higher plasma levels of radioactivity in Gunn rats adds support to the concept of reduced formation of the conjugates. 17 references. (Author abstract modified)

001135 Baker, G. B.; Bertolini, A.; del Carmine, R.; Martin, I. L.; Raiteri, M. MRC Neuropharmacology Unit, The Medical School, Birmingham, England **Effects of p-chloro-beta-phenylethylamine on the uptake and release of putative amine neurotransmitters in rat brain.** *British Journal of Pharmacology* (London). 58(3):420P-421P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of p-chloro-beta-phenylethylamine (PCPE) on the uptake and release of dopamine (DA), noradrenaline (NA), and 5-hydroxytryptamine (5-HT) in the rat brain. PCPE was found to be a much more potent inhibitor of 5-HT and NA uptake than of DA uptake as indicated by incubation of rat brain fractions with tritiated amines. There were marked differences in stimulation of amine release with particularly strong stimulation of 5-HT release. This compound appears to be useful for studying structure/activity relationships in the effects of phenylethylamine derivatives on the transport of amine neurotransmitters. 5 references.

001136 Beckman, Alexander L.; Stanton, Toni L. Dept. of Physiology, University of Pennsylvania, Philadelphia, PA 19174 **Changes in CNS responsiveness during hibernation.** *American Journal of Physiology*. 231(3):810-816, 1976.

The ability of the golden mantled ground squirrel (*Citellus lateralis*) midbrain reticular formation (MRF) to produce thermogenic responses and to trigger arousal from hibernation was tested during successive quarters of individual hibernation bouts. The animals were implanted with bilateral cannula guides into the MRF. Single, bilateral injections of acetylcholine (ACh) were delivered in each quarter of the same bout or in selected quarters of different bouts. The results show that the magnitude of thermogenic responses evoked by ACh stimulation of the MRF was depressed during the early portion of the bout and increased as time in the bout elapsed. Furthermore, the magnitude of responses evoked during hibernation was depressed in comparison to those evoked during euthermia, indicating the influence of inhibition on the responsiveness of the CNS during hibernation. It is suggested that during hibernation, a progressive change in responsiveness of the CNS, perhaps focused in the MRF, controls the duration of each hibernation bout. 41 references. (Author abstract modified)

001137 Belin, Marie-Francoise; Kouyoumdjian, J.-C.; Barakdjian, Josiane; Duhault, J.; Gonnard, P. Departement de Biochimie, Centre Hospitalier Universitaire Henri Mondor, F-

94010 Creteil Cedex, France **Effects of fenfluramine on accumulation of 5-hydroxytryptamine and other neurotransmitters into synaptosomes of rat brain.** *Neuropharmacology* (Oxford). 15(10):613-617, 1976.

The effects of fenfluramine on the uptake of 5-hydroxytryptamine (5-HT), dopamine (DA), and gamma-n-aminobutyric acid (GABA) or their precursors tryptophan, tyrosine, and glutamic acid into synaptosomes of rat brain were investigated. In vivo, fenfluramine is a competitive inhibitor of the high affinity synaptosomal uptake of 5-HT. Fenfluramine produced a small reduction in the uptake of DA, GABA, and glutamic acid. In vitro, addition of fenfluramine into a synaptosomal fraction reduced uptake of 5-HT, DA, GABA, glutamic acid, tryptophan, and tyrosine. Radiolabeled fenfluramine itself was bound to synaptosomes. Ten days after 5,6-dihydroxytryptamine treatment, both the accumulation of radiolabeled fenfluramine in the brain in vivo and the binding of radiolabeled fenfluramine to synaptosomes in vitro were reduced. It is suggested that 5-HT synaptosomal sites are involved in some actions of fenfluramine. 28 references. (Author abstract modified)

001138 Bending, M. R.; Bennett, P. N.; Rowland, M. Department of Clinical Pharmacology, Royal Postgraduate Medical School, London, England **Pethidine pharmacokinetics in dog: dose and time studies.** *British Journal of Pharmacology* (London). 58(3):472P-473P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effect of dose and time on the oral availability and disposition kinetics of pethidine in greyhound dogs. Terminal half-life of the blood/concentration/time curve increased with dose following an apparently nonlinear relationship, becoming increasingly disproportionate at higher doses. However, the volume of distribution was a constant, indicating that changes in terminal disposition rate reflect changes in clearance. Clearance approached liver blood flow and low oral availability is compatible with significant first pass hepatic metabolism of pethidine. The data suggest that while pethidine may exhibit dose dependent disposition kinetics, there is no apparent evidence for time dependent kinetics at the doses studied. 2 references.

001139 Berkowitz, Barry A.; Ngai, S. H.; Finck, A. Donald. Roche Institute of Molecular Biology, Nutley, NJ 07110 **Nitrous oxide "analgesia": resemblance to opiate action.** *Science*. 194(4268):967-968, 1976.

In order to characterize the nature of nitrous oxide analgesia, mice were intraperitoneally injected with phenylquinone. Nitrous oxide was found to inhibit writhing, producing a dose related analgesia. Narcotic antagonists or chronic morphinization reduced nitrous oxide analgesia. Either nitrous oxide releases an endogenous analgesic or narcotic antagonists have analgesic antagonist properties heretofore unappreciated. 9 references. (Author abstract modified)

001140 Bernasconi, S.; Garattini, S.; Samanin, R. Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea, 62, I-20157 Milano, Italy **The effect of steroid contraceptives on the concentrations of brain monoamines in rats and mice.** *Archives internationales de Pharmacodynamie et de Therapie* (Ghent). 222(2):272-281, 1976.

The effect of three estrogen/progestin combinations on biogenic amines in discrete brain areas of rats and mice was investigated. No significant changes in the levels of serotonin, noradrenaline or dopamine in the rat brain were found follow-

ing the administration of the compounds under study. In mice moderate but significant changes in the levels of serotonin, dopamine, noradrenaline and 5-hydroxyindolacetic acid were found in various brain areas depending on the estrogen-progestin combination used. The potential importance of these effects for the contraceptive as well as for some central actions of these compounds is discussed. 19 references. (Author abstract modified)

001141 Bevan, P.; Bradshaw, C. M.; Szabadi, E. Department of Psychiatry, University of Manchester, Stopford Building, Oxford Rd., Manchester M13 9PT, England **Neuronal responses to adrenoceptor agonists in the cerebral cortex: evidence for excitatory alpha-adrenoceptors and inhibitory beta-adrenoceptors**. *British Journal of Pharmacology* (London). 58(3):418P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of alpha-adrenoceptor and beta-adrenoceptor agonists on cortical neurons of rats. Noradrenaline caused cellular excitation 66% of the time and cellular depression 34% while isoprenaline produced 28% excitation and 72% depression and phenylephrine 100% excitation. Excitatory responses of noradrenaline were reversed by phentolamine, phenoxylbenzamine and propranolol. Those of isoprenaline were reversed by phenoxylbenzamine and sotalol and those of phenylephrine by phenoxylbenzamine. Depressant responses to isoprenaline were antagonized by sotalol. Responses to acetylcholine were unaffected. Results suggest that the same cortical neuron may respond with excitation and depression to adrenoceptor agonists with the excitatory responses probably mediated by alpha-adrenoceptors and the depressant responses mediated by beta-adrenoceptors. 4 references.

001142 Bevan, P.; Bradshaw, C. M.; Szabadi, E. Department of Psychiatry, University of Manchester, Stopford Building, Oxford Road, Manchester, M13 9PT, England **The action of microelectrophoretically applied L-3,4-dihydroxyphenylalanine (DOPA) on single cortical neurones**. *British Journal of Pharmacology* (London). 58(2):239-245, 1976.

The technique of microelectrophoresis was used to compare the actions of L-3,4-dihydroxyphenylalanine (DOPA) and noradrenaline on single neurones in the cerebral cortices of cats and rats. DOPA could both excite and depress cortical neurones. Cells excited by DOPA were also excited by noradrenaline and cells depressed by DOPA were also depressed by noradrenaline. In the case of both excitatory and depressant responses, DOPA appeared to be less potent than noradrenaline. Responses to DOPA and noradrenaline could be antagonized by phentolamine and propranolol. Responses to acetylcholine were not affected. Responses to acetylcholine, but not responses to DOPA, were antagonized by atropine. The results indicate that locally applied DOPA may mimic the actions of noradrenaline on cortical neurones. Possible mechanisms for these effects of DOPA are discussed. 20 references. (Author abstract)

001143 Bhattacharya, S. K.; Mukhopadhyay, S. N.; Reddy, P. K. S. P.; Das, P. K. Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India **Role of brain monoamines in the anticonvulsant effect of imipramine in albino rats**. *Pharmacology* (Basel). 14(5):428-434, 1976.

The role of brain monoamines in the anticonvulsant effect of imipramine was investigated in albino rats, against maximal electroshock induced seizures, by using drugs with well

defined effects on brain monoamines, such as reserpine, 6-hydroxydopamine, alpha-methyl-p-tyrosine, alpha-methyl-dopa, diethyldithiocarbamate, p-chlorophenylalanine, propranolol, phenoxylbenzamine, methysergide, haloperidol, L-dopa, 5-hydroxytryptophan, and apomorphine. Results suggest a definite role for noradrenaline in imipramine anticonvulsant action. Dopamine and 5-hydroxytryptamine do not appear to be involved in this effect of imipramine. 39 references. (Author abstract modified)

001144 Bielicki, L.; Krieglstein, J. no address **Decreased GABA and glutamate concentration in rat brain after treatment with 6-aminonicotinamide**. *Naunyn-Schmiedeberg's Archives of Pharmacology* (Berlin). 294(2):157-160, 1976.

The effects of 6-aminonicotinamide (6-AN) on glutamate, GABA and aspartate in rat brain were investigated. Alterations in the cerebral energy metabolism after 6-AN application included increased levels of glucose and glucose-6-phosphate and decreased levels of lactate and pyruvate and could be interpreted as the result of a reduced glycolytic flux rate. After a prolonged period of 6-AN treatment, GABA and glutamate concentrations were significantly reduced but the level of aspartate was unchanged. It is suggested that changes in the concentration of GABA and glutamate could be responsible for some of the neurological symptoms produced by 6-AN. 21 references. (Author abstract modified)

001145 Biggio, G.; Guidotti, A. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeth's Hospital, Washington, DC 20032 **Climbing fiber activation and 3',5'-cyclic guanosine monophosphate (cGMP) content in cortex and deep nuclei of cerebellum**. *Brain Research* (Amsterdam). 107(2):365-373, 1976.

The role of cyclic 3',5'-guanosine monophosphate (cGMP) in the cerebellum was studied using 3-acetylpyridine (3-AP) which destroys the climbing fibers and leaves intact the mossy fibers. Harmaline cold exposure or isoniazid increased the cGMP content in rat cerebellar cortex. Isoniazid but not harmaline or cold exposure increased cGMP in the deep cerebellar nuclei (nuclei interpositus, vestibularis and fastigii) and striatum. In rats treated with the nicotinamide antagonist 3-AP the tremorogenic effect of harmaline and the increase of cerebellar cortex cGMP produced by this alkaloid was abated. Similarly the increase of cGMP following exposure to cold was reduced. In contrast isoniazid and glutamate increased cGMP to the same extent in control and 3-AP treated rats. It is suggested that an increase of cGMP content in postsynaptic cerebellar elements (presumably Purkinje cells) may be an expression of an increased release of an excitatory transmitter from either the climbing fibers or the parallel fibers. 24 references. (Author abstract modified)

001146 Bigler, Erin D.; Eidelberg, Eduardo. Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, Phoenix, AZ 85013 **Principal cells in lateral geniculate: effects of metrazol on capacity to after-discharge**. *Brain Research Bulletin*. 1(5):485-487, 1976.

The effect of metrazol on the capacity of dorsal lateral geniculate nucleus (dLGN) principal (P) cells to repetitively burst (afterdischarge) following visual system stimulation was examined in P-cells which differed in terms of response patterns to visual stimulation (latency of initial spike, extent of repetitive bursting, and on type or off type responding cells). Twenty seven P-cells were examined in rats (N=27). Metrazol augmented repetitive bursting irrespective of the type of P-cell as long as repetitive bursting was present in the premetrazol

period. P-cells that displayed only a single initial burst to photic stimulation did not exhibit afterdischarge bursting during the metrazol challenge. In all but one cell metrazol enhanced baseline firing rate. These results are discussed in terms of the putative nature of inhibition in the rat dLGN. 22 references. (Author abstract)

001147 Birdsall, N. J. M.; Bradbury, A. F.; Burgen, A. S. V.; Hulme, E. C.; Smyth, D. G.; Snell, C. R. National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Interactions of peptides derived from the C-fragment of beta-lipotropin with brain opiate receptors.** *British Journal of Pharmacology* (London). 58(3):460P-461P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the interactions of peptides derived from the C-fragment of with brain opiate receptors. C-fragment is a 31 residue peptide which appears to have a high affinity for brain opiate receptors and competes equally well for binding sites against naloxone and dihydromorphine. Removal of residues 30 and 31 had little effect on binding properties, but further removal of residues 28 and 19 reduced the affinity by a factor of 20. Investigations of the N-terminal binding region of the fragment showed that methylation or amidization of methionine enkephalin sequence increased overall affinity without affecting the morphine like binding properties of met-enkephalin. However, other substitutions such as benzoylation or amino acid substitution reduces potency against naloxone by 30 fold and produces an even larger effect on the potency against dihydromorphine. Although the binding properties of C-fragment resemble those of alkaloid antagonists, it seems to have potent central analgesic properties. The presence of two binding sites for C-fragment may account for combination of properties. 4 references.

001148 Blasig, J.; Herz, A. Max-Planck-Institut für Psychiatrie, Abteilung für Neuropsychiatrie, Kraepelinstrasse 2, D-8000 München 40, West Germany **Tolerance and dependence induced by morphine-like pituitary peptides in rats.** *Naunyn-Schmiedeberg's Archives of Pharmacology* (Berlin). 294(3):297-300, 1976.

An extract from porcine pituitaries containing peptides with opiate like activity (endorphins) was investigated for possible tolerance/dependence liability in rats. Rats made tolerant to morphine by repeated pellet implantation proved cross-tolerant to the pituitary extract as well as to synthetic methionine enkephalin. Naloxone given to rats, repeatedly pretreated with endorphins, precipitated a withdrawal syndrome strongly resembling that induced in rats treated with normorphine. Results suggest that identical sites and mechanisms are involved in the development of tolerance/dependence induced by opiates and pituitary endorphins. 14 references. (Author abstract modified)

001149 Bloom, Emanuel M.; Hamill, Robert W.; Black, Ira B. Laboratory of Developmental Neurology, Department of Neurology, Cornell University Medical College, New York, NY 10021 **Elevation of tyrosine hydroxylase activity in sympathetic neurons after reserpine: the role of the central nervous system.** *Brain Research* (Amsterdam). 115(3):525-528, 1976.

Rats were subjected to spinal transection, and groups were treated with reserpine 24 hours later, to determine the role of central nervous system pathways in the induction of tyrosine hydroxylase (T-OH) in the sixth lumbar (L-6) ganglion. Forty eight hours after injection, T-OH activity was determined. As expected reserpine treatment resulted in a significant increase in T-OH activity in animals with intact spinal cords. However,

spinal transection prevented the reserpine induced rise in enzyme activity. Interruption of pathways within the central nervous system blocked the induction of T-OH activity in L-6 sympathetic ganglia. Since this ganglion is innervated by spinal segments caudal to the lesion, central pathways appear necessary for the enzyme induction. These observations imply that transsynaptic induction of T-OH in peripheral sympathetic neurons is mediated by higher centers in the central nervous system. This contention is consistent with the observation that electrical stimulation of the brain is associated with an increase in adrenal T-OH activity. Consequently, the preganglionic, intermediolateral column neurons apparently require information of suprasegmental origin in the regulation of T-OH induction in the periphery. 14 references.

001150 Bockaert, J.; Premont, J.; Glowinski, J.; Thierry, A. M.; Tassin, J. P. Laboratoire de Physiologie Cellulaire, Collège de France, F-75231 Paris Cedex 5, France **Topographical distribution of dopaminergic innervation and of dopaminergic receptors in the rat striatum. II. Distribution and characteristics of dopamine adenylate cyclase - interaction of D-LSD with dopaminergic receptors.** *Brain Research* (Amsterdam). 107(2):303-315, 1976.

The characteristics of dopamine adenylate cyclase in the rat striatum was studied on homogenates of fresh rat striatal tissue. Dopamine stimulated the enzyme activity by 250%. This effect was completely blocked by fluphenazine and by phenolamine. LSD stimulated the adenylate cyclase activity by interacting with dopamine receptors. Isoproterenol activated an adenylate cyclase through a receptor distinct from the dopaminergic receptor; this stimulation was not affected by fluphenazine or phenolamine but was suppressed by propranolol. The topographical distribution of the dopamine, LSD and isoproterenol adenylate cyclase activities were examined in homogenates prepared from discs punched out on serial frozen slices of striatum. The dopamine maximal stimulation was 150%. The topographical curves of maximal activation of adenylate cyclase by dopamine and LSD were superimposable confirming that LSD acts on dopaminergic receptors. The topographical distribution of dopamine sensitive adenylate cyclase is comparable to that of endogenous dopamine and to that of the dopamine high affinity uptake activity. In contrast to that observed with dopamine or LSD, the topographical distribution of the adenylate cyclase sensitive to isoproterenol was homogenous within the striatum. 25 references. (Author abstract modified)

001151 Bockaert, J.; Tassin, J. P.; Thierry, A. M.; Glowinski, J.; Premont, J. Lab. of Physiology, INSERM U. 114, 11 Marcelin Berthelot Place, F-75231 Paris Cedex 5, France **Characteristics of dopamine and beta-adrenergic sensitive adenylate cyclases in the frontal cerebral cortex of the rat. Comparative effects of neuroleptics on frontal cortex and striatal dopamine sensitive adenylate cyclases.** *Brain Research* (Amsterdam). 122(1):71-86, 1977.

The effects of dopamine on adenylate cyclase activity were estimated in frontal cerebral cortex homogenates of the rat, and these effects were compared to those induced by L-isoproterenol and L-norepinephrine and various neuroleptics. Fluphenazine was more potent in blocking the striatal than the frontal cerebral cortex dopaminergic receptors. In contrast, haloperidol had a higher affinity for the cerebral frontal cortex than for the striatal dopaminergic receptors. Thus, haloperidol was less effective than fluphenazine in blocking the striatal dopaminergic receptors, and equally potent to fluphenazine in inhibiting the frontal cerebral cortex dopamine sensitive

adenylate cyclase. Chlorpromazine, thioridazine, and clozapine had the same affinity for the two dopaminergic adenylate cyclase systems. L-isoproterenol interacted with a homogeneous population of beta-adrenergic receptor sites coupled with an adenylate cyclase distinct from the dopamine sensitive adenylate cyclase. This beta-receptor had no affinity for dopamine or fluphenazine but was blocked by propranolol or pindolol. L-norepinephrine was shown to stimulate both the dopamine and the beta-adrenergic sensitive adenylate cyclases. Thus, the L-norepinephrine effect was totally blocked in the combined presence of fluphenazine and pindolol. 38 references. (Author abstract modified)

001152 Bowers, Malcolm B., Jr.; Rozitis, Angelika. Yale University School of Medicine, 333 Cedar Street, New Haven CT 06510 Brain homovanillic acid: regional changes over time with antipsychotic drugs. *European Journal of Pharmacology* (Amsterdam). 39(1):109-115, 1976.

The development of tolerance to antipsychotic drugs as measured by levels of brain homovanillic acid (HVA) in different regions of the brain was studied in the rabbit. Acute administration of equivalent doses of chlorpromazine, thioridazine, or clozapine produced progressively smaller increases in brain HVA; however, changes in HVA in three brain regions were of equal magnitude for a single dose of a given drug. Chronic administration of fluphenazine enanthate resulted in a decrease in HVA relative to acute treatment in caudate more than limbic regions. No differences between caudate and limbic regions were observed during daily chlorpromazine administration for 3 or 8 days. Tolerance appeared to develop in approximately 1 week. Chronic treatment with clozapine produced no tolerance at 1 week but suggestive evidence of tolerance in caudate and limbic regions appeared at 2 weeks. No tolerance was observed in the hypothalamus during chronic treatment with any drug used. Cisternal CSF HVA paralleled caudate HVA during acute and chronic treatments. 18 references. (Author abstract modified)

001153 Bowery, N. G. Department of Pharmacology, St. Thomas' Hospital Medical School, London SE1 7EH, England Reversal of the action of gamma-aminobutyric acid (GABA) antagonists by barbiturates. *British Journal of Pharmacology* (London). 58(3):456P-457P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed reversal of the action of GABA antagonists by barbiturates in the rat by recording sympathetic ganglion cell depolarization in the isolated desheathed superior cervical ganglion. GABA responses depressed by bicuculline methochloride were restored by the simultaneous addition of sodium pentobarbitone. Pentobarbitone alone depressed responses to both GABA and carbachol. Pentobarbitone also reversed the effects of other GABA antagonists such as picrotoxin and tetramethylethylsulfotetramine, but did not reverse the antagonistic effect of hexamethonium against carbachol. Thiopentone and amylobarbitone were as active as pentobarbitone with hexobarbitone and butobarbitone less active and barbitone and phenobarbitone inactive. 7 references.

001154 Braestrup, Claus; Scheel-Kruger, Jorgen. Psychopharmacological Research Laboratory, Sct. Hans Hospital, Dept. E., DK-4000 Roskilde, Denmark Methylphenidate-like effects of the new antidepressant drug nomifensine (HOE 984). *European Journal of Pharmacology* (Amsterdam). 38(2):305-312, 1976.

The mechanism of action of nomifensine, a drug with antidepressant properties, and two of its metabolites, M1 and

M2, was examined in rats and compared with dextroamphetamine, methylphenidate, apomorphine, cocaine, and benzotropine. Nomifensine induced stereotyped behavior was completely antagonized by pretreatment with reserpine but not by short time pretreatment with alphamethyltyrosine. Nomifensine thus differs from dextroamphetamine and apomorphine but resembles methylphenidate on stereotyped behavior. Nomifensine, M1, methylphenidate and dextroamphetamine induced a strong increase in the brain level of homovanillic acid (HVA), whereas the dopamine uptake inhibitor benzotropine induced no changes in HVA and cocaine induced only a small increase. Nomifensine, M1 and methylphenidate increased 3,4-dihydroxyphenylacetic acid (DOPAC) whereas amphetamine, apomorphine, benzotropine and cocaine decreased this dopamine metabolite. It is suggested that the stereotyped licking and/or biting activity in the rat is related to the dopamine releasing properties of nomifensine, methylphenidate, and amphetamine. 24 references. (Author abstract modified)

001155 Brunelli, M.; Castellucci, V.; Kandel, E. R. Div. of Neurobiology and Behavior, College of Physicians and Surgeons of Columbia University, NY 10032 Synaptic facilitation and behavioral sensitization in Aplysia: possible role of serotonin and cyclic AMP. *Science*. 194(4270):1178-1181, 1976.

To analyze the molecular mechanisms underlying the presynaptic facilitation at monosynaptic connections between sensory neurons and motor cells accompanying sensitization of the gill withdrawal reflex in the marine mollusk Aplysia, the pharmacological actions of serotonin, octapamine, and dopamine were examined. Only serotonin enhanced synaptic transmission between the sensory and the motor neurons. A serotonin antagonist, cinanserin, reversibly blocked the synaptic facilitation. The action of serotonin may be mediated by adenosine 3',5'-monophosphate (cyclic AMP); exposing the ganglion to dibutyryl cyclic AMP or injecting cyclic AMP into the cell body enhances the synaptic action of a sensory neuron. The mechanism of presynaptic facilitation, therefore, may include activation of one or more serotonergic neurons, which enhance the release of a neurotransmitter by increasing the intracellular concentration of cyclic AMP in the terminals of the sensory neurons. (Author abstract modified)

001156 Buckholtz, Neil S.; Boggan, William O. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29401 Effects of tetrahydro-beta-carbolines on monoamine oxidase and serotonin uptake in mouse brain. *Biochemical Pharmacology* (Oxford). 25(20):2319-2321, 1976.

The effects of 6-methoxy-1,2,3,4-tetrahydro-beta-carboline (6-MeO-THBC) and tetrahydro-norharman on mouse brain monoamine oxidase (MAO) activity and on serotonin (5-hydroxytryptamine, 5-HT) uptake were investigated. Tetrahydro-norharman and 6-MeO-THBC both inhibited MAO in vitro and inhibited 5-HT uptake in vitro and in vivo. The uptake inhibition takes place at a lower concentration than MAO inhibition and thus seems to be the stronger effect. It is suggested that the hallucinogenic effects of many of the beta-carbolines may be related to the effects of these compounds on 5-HT metabolism. 23 references.

001157 Bunag, Ruben D.; Riley, Elinor; Montello, Margie. Department of Pharmacology, University of Kansas Medical Center, Kansas City, KS 66103 Sustained pressor responsiveness to prolonged hypothalamic stimulation in awake rats. *American Journal of Physiology*. 231(6):1708-1715, 1976.

Whether or not pressor responsiveness changes in unanesthetized rats during recurrent sympathetic excitation was determined by recording blood pressure and heart rate continuously while the posterior hypothalamus was stimulated repeatedly with constant currents. Because preliminary tests showed that telestimulation with a radio controlled stimulator produced erratic responses, awake rats were routinely stimulated in a conventional manner by connecting them through wires to a square wave stimulator. Although tachycardia was the most common chronotropic effect, bradycardia also occurred, and both responses were occasionally seen in the same rat at different times. Inhibition of chronotropic responses by combined pharmacologic blockade with propranolol and atropine did not affect corresponding pressor responses in normotensive rats. Renal and spontaneously hypertensive rats always had larger pressor responses than normotensive ones, and, in spite of individual variations, responsiveness generally remained unaltered during 3 to 6 h of repeated hypothalamic stimulation. These results indicate that in awake normotensive or hypertensive rats cardiovascular responses to posterior hypothalamic stimulation continue unabated even when stimulation is repeated for hours. 20 references. (Author abstract)

001158 Burkard, W. P.; Pieri, L.; Haefely, W. F. Hoffmann-LaRoche & Co. Ltd., Department of Experimental Medicine, CH-4002 Basel, Switzerland *In vivo* changes of guanosine 3',5'-cyclic phosphate in rat cerebellum by dopaminergic mechanisms. *Journal of Neurochemistry* (Oxford). 27(1):297-298, 1976.

Experiments indicating that dopamine receptor stimulation and blockade elevate and reduce the content of guanosine 3',5'-cyclic phosphate (cGMP) in the cerebellum of the rat are discussed. Apomorphine produced a dose dependent increase of the cGMP level in the cerebellum 30 min after intraperitoneal administration. The effect of apomorphine reached a peak about 15 min after administration, and after 2 hr the levels of cGMP were back to control values. Results indicate that apomorphine and LSD elevate cGMP in the cerebellum of the rat. It is concluded that dopamine receptor stimulation by apomorphine and LSD results in the activation of a cholinergic system. 13 references.

001159 Burki, H. R.; Sayers, A. C.; Ruch, W.; Asper, H. Forschungsinstitut Wander, Postfach 2747, Bern, Switzerland *Influence of anticholinergics and clozapine on the haloperidol induced activation of the dopaminergic system in the striatum of the rat: neurochemical results.* Einfluss von Anticholinergika sowie Clozapin auf die durch Haloperidol induzierte Aktivierung des dopaminergen Systems im Striatum der Ratte: Neurochemische Ergebnisse. *Arzneimittel-Forschung* (Aulendorf). 26(6):1094-1096, 1976.

The interaction between haloperidol and anticholinergics was studied in the rat brain. Atropine reduced the content of homovanillic acid (HVA) in the striatum and partially prevented the rise of HVA induced by oxotremorine or low doses of haloperidol; however, the effect of high doses of haloperidol on the rise of HVA was unaffected. When haloperidol was administered for 6 days, the increase of HVA on days 3 to 6 was diminished, and 27 hr after the last dose of haloperidol the content of HVA fell below the control value and remained below it for a week. Clozapine did not prevent the HVA increase induced by oxotremorine or haloperidol. The effects of haloperidol are probably due to a functional modification of the striatal dopamine receptors following repeated administration. 5 references.

001160 Cahill, Anne L.; Medzihradsky, Fedor. University of Michigan Medical Center, Ann Arbor, MI 48109 *Interaction of central nervous system drugs with synaptosomal transport processes.* *Biochemical Pharmacology* (Oxford). 25(20):2257-2264, 1976.

Interaction of a wide range of CNS drugs with the transport of 5-hydroxytryptamine (5-HT) and norepinephrine (NE) into synaptosomes from cerebral cortex of rats was investigated. The interaction of these drugs with the synaptic transport of sodium and potassium was also assessed. Although of different numerical value, the order of potency of the drugs in inhibiting the uptakes of both biogenic amines was comparable. Similar inhibition constants were obtained for the low affinity uptake of 5-HT and the uptake of NE. Desipramine and amphetamine strongly inhibited both uptake processes. Levorphanol strongly inhibited 5-HT uptake; this effect was not stereospecific. Methadone and pentazocine were strong inhibitors, but morphine, codeine and naloxone were markedly weak inhibitors. The uptake of both 5-HT and NE was strongly inhibited by quinacrine. Only methadone showed substantial inhibition of synaptosomal Na,K-ATPase. The reversible inhibition of the enzyme by methadone was diminished at concentrations of Na and K reflecting synaptic discharge. Methadone partially bound to the ouabain site of the enzyme and also inhibited the Mg activated component. The feasibility and experimental conditions were established for using a modified crude mitochondrial fraction as synaptosomal preparation to study transport processes in general and the uptake of biogenic amines in particular. 59 references. (Author abstract modified)

001161 Cankat Tulunay, F. Department of Pharmacology, Medical School of Ankara University, Sıhhiye, Ankara, Turkey *The effect of lithium chloride on morphine- and pyrogen-induced hyperthermia in rats.* *Pharmacology* (Basel). 14(5):422-427, 1976.

Hyperthermia was produced in rats with doses of morphine between 2.5 and 20 mg/kg. Dose dependent hypothermia was induced with 50 to 400 mg/kg lithium chloride. Morphine induced and pyrogen induced hyperthermia were inhibited by these doses of lithium chloride. The hypothermic effect of lithium may be due to the replacement of sodium ions by lithium ions in the hypothalamus. The antagonism between morphine and lithium is seen to be nonspecific. 24 references. (Author abstract modified)

001162 Carey, Robert J. Veterans Administration Hospital, Syracuse, NY 13210 *Effects of selective forebrain depletions of norepinephrine and serotonin on the activity and food intake effects of amphetamine and fenfluramine.* *Pharmacology Biochemistry and Behavior*. 5(5):519-523, 1976.

Selective forebrain depletions of either norepinephrine or serotonin were produced in separate groups of rats by placement of lesions in the brainstem noradrenergic area and in the dorsal and median raphe nuclei respectively. Rats with norepinephrine depleting lesions exhibited an attenuation relative to intact animals of both the anorexic and locomotor stimulatory effects of amphetamine. In contrast, depletion of serotonin by the raphe lesion enhanced the locomotor stimulation induced by amphetamine but did not affect the anorexic efficacy of amphetamine. Neither brain lesion, however, reliably altered the animals' response to either the anorexic or activity effects of fenfluramine. 16 references. (Author abstract)

001163 Carpenter, J. R.; Faunch, Rosemary. Department of Pharmacology, Materia Medica and Therapeutics, University of Manchester, Manchester M13 9PT, England **Does cocaine have a post-synaptic action on rat anococcygeus muscle?** *Journal of Pharmacy and Pharmacology* (London). 28(9):724-725, 1976.

The hypothesis that uptake inhibition is the mechanism whereby cocaine potentiates responses to noradrenaline in tissues with rich noradrenergic innervations, whereas a postsynaptic action is the mechanism whereby cocaine potentiates responses to noradrenaline in tissues with sparse noradrenergic innervations was tested. The effect of cocaine on responses of isolated rat anococcygeus muscles to supramaximal doses of noradrenaline, both before and after treatment with phenoxybenzamine was examined. Results indicate that, in this preparation, cocaine does not increase the apparent efficacy or intrinsic activity of the noradrenaline α -adrenoceptor interaction. It is suggested that in view of the specialized architecture of the rat anococcygeus muscle, the observed effect is due to increases in the local concentration of noradrenaline. 8 references.

001164 Cedarbaum, Jesse M.; Aghajanian, George K. Department of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, New Haven, CT 06508 **Noradrenergic neurons of the locus coeruleus: inhibition by epinephrine and activation by the α -antagonist piperoxane.** *Brain Research* (Amsterdam). 112(2):413-419, 1976.

The effects of piperoxane on the firing rate of locus coeruleus (LC) neurons alone and in combination with clonidine norepinephrine (NE) and pinephrine (E) were studied in rats in order to investigate the hypothesis that piperoxane may be a specific antagonist and that clonidine may be a specific agonist at E mediated synapses in the CNS. An attempt to characterize the receptor involved was made using isoproterenol (ISO) and sotalol. Piperoxane increases the firing rate of the LC neurons and prevents or reverses the inhibition of these cells by clonidine. Sotalol produces neither of these effects. Administration of E, ISO, NE, and clonidine exhibit the spontaneous firing of LC cells. Piperoxane antagonized this inhibition; sotalol does not. Despite the agonist activity of ISO, the receptor involved at the LC bears a resemblance to the peripheral α -adrenergic receptor. It is suggested that E may function as a neurotransmitter in the mammalian CNS acting at inhibitory synapses upon central NE neurons in the LC. 40 references.

001165 Chalfie, M.; Hoadley, Deborah; Pastan, S.; Perlman, R. L. Dept. of Physiology, Harvard Medical School, 25 Shattuck St., Boston, MA 02115 **Calcium uptake into rat pheochromocytoma cells.** *Journal of Neurochemistry* (Oxford). 27(6):1405-1409, 1976.

The uptake of labeled calcium ion (Ca^{2+}) into cell suspensions prepared from a transplantable rat pheochromocytoma was measured. Results reveal a biphasic uptake pattern with rapid initial uptake followed by slower, linear uptake for at least 10 minutes at 37 degrees C. Ca^{2+} uptake was a linear function of the external Ca^{2+} concentration over the range of 0.13 to 2.5mM. Incubation of the cells in a potassium containing medium caused a 2 to 3 fold increase in Ca^{2+} uptake in both phases. It is suggested that the cells lack a mechanism to inactivate this potassium induced increase in Ca^{2+} permeability. Further findings indicate that diphenylhydantoin and verapamil, inhibitors of potassium stimulated catecholamine secretion, both inhibited potassium induced Ca^{2+} uptake. It is concluded that results provide a direct demonstration of the stimulus coupled uptake of Ca^{2+} into chromaffin cells and

provide additional evidence for the correlation of Ca^{2+} uptake with catecholamine secretion by these cells. 19 references. (Author abstract modified)

001166 Chan, Arthur W. K. Research Institute on Alcoholism, 1021 Main Street, Buffalo, NY 14203 **Gamma aminobutyric acid in different strains of mice. Effect of ethanol.** *Life Sciences* (Oxford). 19(4):597-603, 1976.

To determine if differences in CNS sensitivity to an acute dose of ethanol may be reflected in differences in CNS gamma-aminobutyric acid (GABA) content, four strains of mice (C57BL/6J, DBA/2J, LS, and SS), which differ in their voluntary intake and/or neural sensitivity to ethanol, were examined for GABA contents in various brain regions following an acute dose (4g/kg). Results indicate that a previously documented ethanol induced elevation of GABA in the whole mouse brain is a phenomenon observed in a variety of brain regions. No correlation was observed between GABA contents in the brain and neural sensitivity to ethanol. 23 references. (Author abstract modified)

001167 Chao, Fu-Chuan; Green, Donald E.; Forrest, Irene S.; Kaplan, Joel N.; Winship-Ball, Ann; Braude, Monique. University of San Francisco, Institute of Chemical Biology; Veterans Administration Hospital, 151F, Palo Alto, CA 94304 **The passage of ^{14}C -delta-9-tetrahydrocannabinol into the milk of lactating squirrel monkeys.** *Research Communications in Chemical Pathology and Pharmacology*. 15(2):303-317, 1976.

A study on passage of labeled delta-9-tetrahydrocannabinol (THC) into mothers' milk has been performed using primates. Lactating squirrel monkeys chronically receiving THC orally either two or five times weekly were given a tracer dose of carbon labelled THC mixed with the regular THC. This permitted radioquantitation of the THC in milk specimens collected 1 to 24 hours after administration of the labeled dose. Correlated specimens of urine and feces were also collected individually from mothers and infants and were subjected to radioquantitation and exploratory thin layer chromatography. During the 24 hour observation period, approximately 0.2% of labeled THC appeared in the milk, and 42% and 1% were excreted in feces and urine, respectively. Infants that suckled during the 6 hours immediately after their mothers were administered the labeled compound excreted an average of 0.01% and 0.12% of the mother's dose in the urine and feces, respectively, during the 18 hours after suckling. Results demonstrate probable similar course of events in humans ingesting THC-like drugs. 11 references. (Author abstract modified)

001168 Churyukanov, V. V.; Bilibin, D. P. I Moskovskogo meditsinskogo instituta im. I. M. Sechenova, Moscow, USSR **Influence of narcotic analgesics on cortical control over transmission of impulses along the afferent paths of the sciatic nerve./ Vliyaniye narkoticheskikh anal'getikov na protsess korkovogo kontrolya peredachi impul'sov v afferentnykh putyakh sedalishchnogo nerva.** *Farmakologiya i Toksikologiya* (Moskva). 6:152-155, 1976.

In experiments with cats it was determined that the narcotic analgesics morphine, promedol and phentanyl when introduced intravenously potentiate the inhibition of evoked potentials in specific tracts of the sciatic nerve, as observed during conditioning stimulation of the visual cortex by electrical impulses. The potentiation of inhibitory corticofugal mechanisms under the influence of narcotic analgesics takes place in the medulla oblongata and thalamus. 19 references. (Author abstract modified)

001169 Closse, Annemarie; Hauser, Daniel. Sandoz, Ltd., Pharmaceutical Division, Chemical Research, CH-4002, Basle, Switzerland **Dihydroergotamine binding to rat brain membranes.** *Life Sciences (Oxford)*. 19(12):1851-1864, 1976.

The identification and characterization of a stereospecific, high affinity binding site for dihydroergotamine on rat brain membranes is reported. 3H-Dihydroergotamine, which is used clinically to treat orthostatic hypotension and migraine, binds saturably, reversibly and with high affinity to rat brain membranes. The binding is time, temperature, and pH dependent and is highest in the hippocampus and the corpus striatum. Serotonin was the only neurotransmitter tested capable of inhibiting 3H-dihydroergotamine binding. 29 references. (Author abstract modified)

001170 Consolo, S.; Bianchi, S.; Ladinsky, H. Istituto di Ricerche Farmacologiche "Mario Negri" Via Eritrea, 62-20157 Milan, Italy **Effect of carbamazepine on cholinergic parameters in rat brain areas.** *Neuropharmacology (Oxford)*. 15(11):653-657, 1976.

The action of the antiepileptic drug, carbamazepine, was studied on the cholinergic tetrad (acetylcholine, choline, choline o-acetyltransferase and cholinesterase) in rat brain areas. The drug increased striatal acetylcholine starting at an intraperitoneal dose of 15mg/kg. The maximal increase in striatal acetylcholine of 66%, was produced at 25mg/kg and the effect persisted for at least 120 minutes. This action was selective for the striatum, there being no effect in other brain regions encompassing the mesencephalon, diencephalon, cerebellum, and hippocampus. The hemispheric residuum (after removal of the striatum and hippocampus) showed a 45% increase in acetylcholine but only at the highest dose used, 50mg/kg. The choline level was decreased markedly in both the striatum and hemispheric residuum by carbamazepine at a dose of 25mg/kg. Neither carbamazepine nor its metabolite, carbamazepine-10, 11-epoxide affected striatal choline o-acetyltransferase or cholinesterase after in vitro incubation. The increase in striatal acetylcholine by carbamazepine was not mediated through the dopaminergic system, since pretreatment with pimozide, a powerful dopaminergic antagonist, did not prevent the effect. No tolerance to the action of carbamazepine on striatal acetylcholine was produced after chronic treatment with 25mg/kg twice per day for 6 days. 28 references. (Author abstract)

001171 Corcoran, Michael E.; Wada, Juhn A.; Wake, Akira; Urstad, Harald. Division of Neurological Sciences, University of British Columbia, 2075 Westbrook Place, Vancouver, B.C., V6T 1W5, Canada **Failure of atropine to retard amygdaloid kindling.** *Experimental Neurology*. 51(1):271-275, 1976.

In light of previous findings that atropine retards the development of kindled amygdaloid seizures, the hypothesis that cholinergic circuitry may participate in the development of amygdaloid seizures but not in the expression of such seizures after they are established, was tested in rats and cats. Rats were kindled with either sine waves or square waves, and half the rats in each group received atropine sulfate i.p. 60 minutes before kindling sessions. Control rats were given distilled water. Injections of water or atropine followed by amygdaloid stimulation were given every 48 hours to minimize any cumulative toxicity of atropine. Cats were kindled with sine waves and were given atropine sulfate i.p. 2 hours before kindling. Results reveal that, in rats, rate of seizure development was independent of waveform and that atropine did not produce a prophylactic effect on amygdaloid kindling.

Atropine administration had no effect on either intensity or duration of seizures. It also failed to suppress amygdaloid kindling in cats. Implications of the discrepancy between these and previous findings are discussed. 17 references.

001172 Correa, F. M. A.; Graeff, F. G. Department of Pharmacology, Faculty of Medicine of Ribeirao Preto, University of Sao Paulo, Sao Paulo, Brazil **On the mechanism of the hypertensive action of intraseptal bradykinin in the rat.** *Neuropharmacology (Oxford)*. 15(11):713-717, 1976.

It was previously suggested that the hypertensive response to intracerebroventricular injections of bradykinin in the rat was mediated by alpha-adrenergic as well as histaminergic mechanisms, and that the lateral septal areas was one site of action of intracerebrally injected bradykinin. In the recent study the role played by alpha-adrenergic and histaminergic mechanisms within the septal area in the bradykinin induced blood pressure rise was studied by using locally administered drug antagonists. The intraseptal injection of bradykinin in rats anaesthetized with urethane caused a dose dependent increase in blood pressure. A hypertensive effect also followed the intraseptal injection of histamine, whereas hypertensive as well as hypotensive responses were observed after intraseptal injection of noradrenaline. The blood pressure rise following intraseptal bradykinin was blocked or even reversed by pretreatment with intraseptal phentolamine but not affected by the same dose of pyrilamine. The blood pressure rise caused by a second injection of intraseptal histamine in the same animal was smaller than that caused by the first injection of equal dose. In addition, the blood pressure response to the first injection of histamine was markedly reduced by pretreatment with intraseptal pyrilamine. These results indicate that the hypertensive response caused by intracerebrally injected bradykinin is mediated by alpha-adrenergic but not histaminergic mechanisms operating within the septal area. 9 references. (Author abstract)

001173 Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Some new vistas on neuronal communication mechanisms: impact on the neuropharmacology of GABA transmission.** (Unpublished paper). SMR-IR-MH, NIMH, 1976.

Novel concepts on dendrodendritic transmission as an important mechanism in the exchange of information between neurons are presented and discussed. Biochemical parameters that may be used to quantify dendrodendritic transmission in discrete brain nuclei are considered in relation to studies of the effects of morphine, haloperidol, apomorphine, 3-acetylpyridine, diazepam, harmaline and muscimol on gamma-aminobutyric acid (GABA) receptors. 25 references.

001174 Cott, J.; Carlsson, A.; Engel, J.; Lindqvist, M. Department of Pharmacology, University of Ibadan, Ibadan, Nigeria **Suppression of ethanol-induced stimulation by GABA-like drugs.** *Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin)*. 295(3):203-209, 1976.

The effects of gamma-hydroxybutyric acid, baclofen and aminooxyacetic acid, which augment or mimic the action of gamma-aminobutyric acid (GABA), on the increase in spontaneous locomotor activity produced in mice by intraperitoneal injection of ethanol were investigated. The ethanol induced, locomotor stimulation was completely eliminated by pretreatment with these agents. Baclofen caused an initial increase in catecholamine synthesis, followed by a later decrease, in dopamine (DA) rich areas of rat brain. The data are consistent with previous findings that baclofen, as well as other agents

which enhance the activity of GABA systems, reduce the firing of DA neurons, causing enhanced synthesis of DA via feedback mechanisms. The findings also indicate a potential interaction between GABA like drugs and alcohol in man. It is suggested that the interaction of GABA like drugs and ethanol may be of heuristic value in the treatment of chronic alcoholism. The possibility that the mechanism of the inhibition of ethanol induced locomotor stimulation by GABA like drugs may be due to a selective interference with ethanol induced DA release is discussed. 49 references. (Author abstract modified)

001175 Cramer, H.; Kiessling, M. Neurologische Universitätsklinik, Hansastrasse 9, D-7800 Freiburg i. Br., Germany /Dopamine sensitive adenylyl cyclase of the brain: effect of L-dopa and piribedil on cAMP concentration in cerebrospinal fluid./ Zur dopaminempfindlichen Adenylzyklase des Gehirns: Wirkung von L-DOPA und Piribedil auf die cAMP-Konzentration im Liquor cerebrospinalis. *Arzneimittel-Forschung* (Aulendorf). 26(6):1106-1107, 1976.

The cerebrospinal fluid (CSF) concentration of cyclic AMP was measured after administration of L-dopa and piribedil (a dopamine receptor stimulator) in male rats weighing 250 to 350g. CSF was obtained by suboccipital puncture. L-dopa, 100 to 200mg/kg, caused a 60% rise in cyclic AMP after 30 min, which returned to normal at the end of 90 min. Piribedil, 10mg/kg, had no effect on cyclic AMP concentration. Flac-63 (bis-(4-methyl-1-homopiperazinyl-thiocarbonyl)-disulfide) partially inhibited the effects of L-dopa or cyclic AMP levels. Propranolol, 10mg/kg, blocked the L-dopa effect on cyclic AMP concentration, while phentolamine, 5mg/kg, had no effect. Phentolamine alone increased cyclic AMP concentration. It is concluded that L-dopa stimulates adenylyl cyclase by a beta-adrenergic receptor. Metabolites of L-dopa could also have a beta-adrenergic effect. 17 references.

001176 Curzon, G.; Fernando, J. C. R. Department of Neurochemistry, Institute of Neurology, Queen Square, London WC1N 3BG, England /Effect of aminophylline on tryptophan and other aromatic amino acids in plasma, brain and other tissues and on brain 5-hydroxytryptamine metabolism. *British Journal of Pharmacology* (London). 58(4):533-545, 1976.

The mechanisms by which aminophylline increase brain tryptophan levels and 5-hydroxytryptamine (5-HT) turnover were investigated in rats. At lower doses, aminophylline increased both the free tryptophan concentration in the plasma and the brain tryptophan concentration. However, the ratio of brain tryptophan to plasma free tryptophan was not significantly altered. A higher dose of aminophylline decreased plasma total tryptophan concentration and increased plasma insulin concentration. The ratio of brain tryptophan to plasma free tryptophan rose considerably. Concentrations of tyrosine and phenylalanine in the brain were not affected. Pretreatment with the beta-adrenergic blocking drug propranolol or the diabetogenic agent streptozotocin prevented aminophylline induced increases in the ratio of brain tryptophan to plasma free tryptophan. It is suggested that changes in brain tryptophan levels after aminophylline may be due to increased availability of plasma tryptophan due to increased lipolysis and increased effectiveness of tryptophan uptake by the brain due to increased insulin secretion. 41 references.

001177 Datta, R. K.; Johnson, E. A.; Bhattacharjee, G.; Stenger, R. J. Department of Pathology, Beth Israel Medical Center, New York, NY 10003 /Influence of acute and chronic administration of methadone hydrochloride on NADPH-

cytochrome c reductase and cytochrome P-450 of mouse liver microsomes. *Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 220(1):86-93, 1976.

Effect of methadone on the activity of NADPH-cytochrome c reductase and the content of cytochrome P-450 of liver microsomes was studied in C57-BL male mice weighing about 30g. Methadone HCl i.p. increased the activity of cytochrome c reductase by 8% and had no effect on cytochrome P-450. When the same dose of methadone was given daily for 5 consecutive days, cytochrome c reductase activity increased 12%, and cytochrome P-450 content increased 10%. There were no differences between male and female mice in the effects of the single acute dose on cytochrome c reductase or cytochrome P-450. Chronic administration of methadone over a 5 week period in increasing doses caused a 30% increase in the activity of cytochrome c reductase. The content of cytochrome P-450 increased with increasing methadone dose until a dose of 29mg/kg was reached, at which time the increase was 15%. Thereafter, increasing the dose of methadone caused a progressive decrease in cytochrome P-450 content until at 40mg/kg methadone, the P-450 content of the microsomes was below that in the control group. Following termination of methadone administration, cytochrome c reductase and cytochrome P-450 levels returned to baseline values within 2 weeks. 24 references.

001178 David, Joy; Grewal, R. S. CIBA-GEIGY Research Centre, Goregaon East, Bombay 400063, India /Effect of carbamazepine (Tegretol) on seizure and EEG patterns in monkeys with alumina-induced focal motor and hippocampal foci. *Epilepsia*. 17(4):415-422, 1976.

Qualitative and quantitative aspects of chronic carbamazepine (Tegretol) medication on focal seizures and associated interictal EEG abnormalities in Rhesus monkeys with alumina induced foci in either the sensorimotor cortex or the hippocampus was investigated. In both groups of animals, carbamazepine produced qualitative control of visible seizures and reduced intracortical spike propagation, but did not cause complete normalization of the background EEG; quantitative indices, such as spike density and amount of paroxysmal discharge representative of abnormal EEG activity, were significantly reduced with respect to predrug values during medication and after cessation as well. Threshold to pentylentetrazol was elevated by carbamazepine in both groups of epileptic monkeys. Aggressivity and other clinical manifestations in monkeys with hippocampal foci were markedly reduced by carbamazepine. 12 references.

001179 Davies, J. Department of Pharmacology, The School of Pharmacy, London WC1N 1AX, England /Effects of morphine and naloxone on renshaw cells and spinal interneurons in morphine dependent and nondependent rats. *Brain Research* (Amsterdam). 113(2):311-326, 1976.

The effects of microelectrophoretically administered morphine, naloxone, levorphanol and dextrorphan on Renshaw cells and interneurons in the spinal cord of morphine dependent and nondependent anaesthetized rats were investigated. Morphine excited cholinergic neurones and enhanced the excitatory actions of acetylcholine and L-glutamate. This action of morphine appeared to be stereospecific and was antagonized by naloxone. Naloxone also antagonized acetylcholine induced excitation but not L-glutamate induced excitation. In dependent rats morphine was a more effective excitant of cholinergic neurones and naloxone was more effective as an antagonist of acetylcholine induced excitations. These observations were interpreted as indicating that

cholinergic mechanisms may be involved in morphine dependence and naloxone precipitated abstinence. 41 references. (Journal abstract)

001180 Day, Alan R.; Lujan, Miguel; Dewey, William L.; Harris, Louis S.; Radding, Jeffrey A.; Freer, Richard J. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Structure-activity relationships of enkephalins in the stimulated guinea pig ileum.** Research Communications in Chemical Pathology and Pharmacology. 14(4):597-603, 1976.

A number of analogs and homologs of methionine-enkephalin were synthesized by the Merrifield method of solid phase peptide synthesis, and each peptide was assayed by inhibition of electrically evoked contraction of the guinea-pig ileum. The minimum sequence required for biological activity in this preparation was found to be the pentapeptide unit. Methionine was readily replaced by norleucine to give an analog with approximately 50% of the potency of the parent compound. Leucine-enkephalin has about 15% to 20% of the potency of the methionine derivative. Modification of the N-terminal tyrosine moiety (that is, substitution by phenylalanine or removal of the amino group) practically abolished activity. Incorporation of O-methyltyrosine into the peptide reduced potency to 1% of the parent compound. The significance of these and other findings in terms of the topography of the guinea-pig ileum receptor site is discussed. 10 references. (Author abstract)

001181 De Saint-Blanquat, G.; Vidaillac, G.; Lindenbaum, A.; Derache, R. Groupe de Recherches sur la Toxicologie des Aliments et des Boissons, INSERM. U. 87, 2 Rue Francois Magendie, 31400 Toulouse, France **Absorption, distribution and excretion of orally administered disulfiram in the rat.** Absorption digestive, fixation tissulaire et excretion du disulfiram administre oralement chez le rat. Archives internationales de Pharmacodynamie et de Therapie (Ghent). 223(2):339-350, 1976.

The absorption, distribution, and excretion of disulfiram and of one of its metabolites, diethyldithiocarbamate, were studied in rats orally treated with disulfiram. Approximately 70% to 90% of the administered dose of disulfiram is absorbed but diethyldithiocarbamate appears in the gut. After absorption, disulfiram and diethyldithiocarbamate impregnate some specific tissues including liver, kidney, and muscle. The blood and brain contain little or no disulfiram. The largest dose of disulfiram decreases fecal bolus and increases urinary volume, probably favoring the excretion of diethyldithiocarbamate. 24 references. (Author abstract modified)

001182 Dell, H.-D.; Fassbender, W.; Kamp, R.; Lorenz, D. Biochemische Abteilung, Troponwerke Dinklage & Co., Berliner Strasse 220-232, D-5000 Cologne 80, Germany **Age and sex dependence of organ distribution and metabolism of chlorprothixene and nortriptyline in rats.** Alters- und Geschlechtsabhängigkeit der Organverteilung und des Metabolismus von Chlorprothixen und Nortriptylin bei Ratten. Arzneimittel-Forschung (Aulendorf). 26(6):1098-1100, 1976.

Organ distribution and metabolism of chlorprothixene and nortriptyline were studied in male and female Wistar rats, 3, 6, and 24 weeks old. The LD-50 of chlorprothixene is about twice as high for 6-week-old rats as for 3-week-old rats, whereas the LD-50 of nortriptyline is about twice as high for 6-week-old rats as for 24-week-old rats. The doses used were 100mg/kg chlorprothixene and 300mg/kg nortriptyline. Animals were sacrificed at 3, 6, 12, 24, 48, or 72 hr after the drug was administered, and the lungs, liver, kidneys, heart, and brain

were examined for the drug and its metabolites. In the case of chlorprothixene, the 3-week-old rats showed greater organ concentration of the drug and slower elimination, and females showed greater organ concentration than the males. With nortriptyline, the 24-week-old animals had greater organ concentration than the 6-week-old animals, and the females had greater organ concentration than the males. In the case of both drugs, the higher concentration was about double the lower concentration, corresponding roughly with the differences in LD-50. 14 references.

001183 Desoize, B.; Jardillier, J. C.; Leger, C.; Nahas, G. G. Laboratoire de Pharmacologie et de Toxicologie Cellulaires, INSERM U-26, 200 rue du Faubourg St. Denis, F-75010 Paris, France **Delta-9-tetrahydrocannabinol (THC) and macromolecular synthesis: mechanisms of action.** British Journal of Pharmacology (London). 58(3):419P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the mechanism of action of the depressant effect of delta-9-tetrahydrocannabinol (THC) on macromolecular synthesis. THC was seen to inhibit the intracellular pool uptake of tritiated leucine, uridine, and thymidine and their incorporation into protein, RNA and DNA. This inhibition of precursor uptake in the cellular pool may explain impairment of macromolecular synthesis and indicates that THC does not exert its inhibitory effect on the synthesis of a specific macromolecule. It appears that the effect is exerted primarily by interfering with the transport enzymes of the plasma membrane and thus may be altering the physicochemical characteristics of the membrane which can effect cell anabolism at every stage of the cell cycle. 3 references.

001184 Dey, P. K.; Feldberg, W. National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Analgesia produced by morphine when acting from the liquor space.** British Journal of Pharmacology (London). 58(3):383-393, 1976.

Analgesia in cats produced by morphine injected into different parts of the liquor space of the brainstem in doses too small to be effective by intravenous injection was studied. Infusions into the fourth ventricle or into the subarachnoid space of doses of 100 to 200 micrograms were sufficient to produce strong long-lasting analgesia. Injection into the cisterna magna required larger doses. It is posited that the site of action of morphine when producing analgesia is the ventral surface of the brainstem. The possibility is discussed that the structures acted upon are tryptaminergic nerve fibers. 33 references. (Author abstract modified)

001185 Diez, James A.; Ward, William G.; Summer, George K. Department of Biochemistry and Nutrition, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Tryptophan transport in brain synaptosomes: effects of L-DOPA.** Brain Research (Amsterdam). 118(3):534-539, 1976.

The effects of L-DOPA on the high affinity uptake of tryptophan and efflux of tryptophan was studied in mouse brain synaptosomal preparations in order to determine whether L-DOPA can directly affect tryptophan transport at the sites of serotonin (5-hydroxytryptamine, 5-HT) synthesis. It was demonstrated that L-DOPA can reduce synaptosomal tryptophan levels by inhibiting the uptake of tryptophan and stimulating the efflux of tryptophan. 24 references.

001186 Dolphin, A.; Jenner, P.; Marsden, C. D. University Department of Neurology, Institute of Psychiatry, Denmark Hill London, SE5 8AF, England **Noradrenaline synthesis from**

L-DOPA in rodents and its relationship to motor activity. Pharmacology Biochemistry and Behavior. 5(4):431-439, 1976.

The extent of involvement of noradrenaline (NA) in the motor activity produced by L-DOPA was studied in normal mice and in those depleted of catecholamines. The time course of induced L-DOPA motor activity was compared with the levels of NA and dopamine (DA) after L-DOPA administration in the presence or absence of the dopamine-beta-hydroxylase inhibitor FLA-63. Cerebral NA levels and DA levels were increased after L-DOPA administration. NA turnover, as determined by increases in 3-methoxy-4-hydroxyphenylglycol sulfate (MOPEG-S04), was also increased. The enhanced NA turnover was related in time to the locomotor response to L-DOPA. FLA-63 prevented the increase in NA and MOPEG-S04 formation following L-DOPA and attenuated the locomotor response to L-DOPA. It is suggested that NA is involved in the production of this response to L-DOPA. 40 references.

001187 Dow, R. C.; Laszlo, I. MRC Brain Metabolism Unit, Department of Pharmacology, University of Edinburgh, 1, George Square, Edinburgh, EH8 9JZ, Scotland **Uptake of 5-hydroxytryptamine in different parts of the brain of the rabbit after intraventricular injection.** British Journal of Pharmacology (London). 56(4):443-447, 1976.

The uptake of 5-hydroxytryptamine (5-HT) was investigated in different areas of the rabbit brain (anterior hypothalamus, the raphe, the region of the substantia nigra, several cortical areas, and the medulla oblongata) after intraventricular injection in pargyline pretreated animals by the formaldehyde induced histochemical fluorescence method. The distribution of fluorescence showed that the uptake of 5-HT, after circulation in the cerebrospinal fluid, caused a general increase in intensity of green yellow to yellow background fluorescence. There was an increased fluorescence in the nerve terminals, but no uptake occurred either in the cell bodies of neurones or in the glial cells. 21 references. (Author abstract)

001188 Draper, A. J.; Grimes, D.; Redfern, P. H. Department of Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, England **The interaction between clonidine and desmethylinipramine: effects on blood pressure and central catecholamine metabolism.** Journal of Pharmacy and Pharmacology (London). 28(Supplement):34P, 1976.

The effect of the antihypertensive drug, clonidine, and desmethylinipramine (DMI), alone and in combination, on blood pressure and norepinephrine metabolism in normotensive rats was studied. DMI, given 20 hr and 6 hr before sacrifice, produced a fall in blood pressure of 12%. Clonidine produced a drop in blood pressure of 20%, but when DMI was given at the end of the period of clonidine treatment, the fall in blood pressure was only 12%. Turnover of norepinephrine was measured in the medulla and hypothalamus by measuring the rate of decline of norepinephrine levels after administration of alpha-methyl-p-tyrosine. Treatment with clonidine alone or DMI alone produced decreases in turnover in the medulla and hypothalamus. Turnover was further decreased by the combination of DMI and clonidine, compared with the decrease produced by clonidine alone. It is suggested that pretreatment with clonidine results in a changed sensitivity of central presynaptic and postsynaptic receptors, such that the accumulated norepinephrine resulting from DMI blockade of reuptake is capable of producing a secondary norepinephrine inhibition. 3 references.

001189 Dray, A.; Gonye, T. J.; Oakley, N. R.; Tanner T. Department of Pharmacology, School of Pharmacy, University of

London, London WC1N 1AX, England **Evidence for the existence of a raphe projection to this substantia nigra in rat.** Brain Research (Amsterdam). 113(1):45-57, 1976.

The effect of electrical stimulation of the median raphe nucleus on the activity of spontaneously firing single neurones in the substantia nigra and mesencephalic reticular formation (MRF) was investigated in rats. Depression of activity was the predominant effect observed, although this was sometimes accompanied by periods of excitation. Some neurones were only excited. The latency of inhibition of substantia nigra neurones was constant whereas that of MRF neurones was more variable. Microiontophoretically applied 5-hydroxytryptamine (5-HT) and dopamine (DA) produced mainly inhibition of neuronal activity, but excitation and biphasic effects were also seen. There was a good correlation between the direction of neuronal responses in the substantia nigra to median raphe stimulation and to the effects of 5-HT, but not to the effects of DA. Discrete electrolytic lesions of the median raphe nucleus were followed by a decrease in 5-HT concentration but not gamma-aminobutyric acid concentration in the substantia nigra. It is suggested that the substantia nigra receives a direct inhibitory input from the median raphe nucleus and this pathway uses a 5-HT like neurotransmitter. This pathway probably contributes to the regulation of nigrostriatal dopaminergic transmission. 28 references. (Author abstract modified)

001190 Dray, A.; Oakley, N. R. Department of Pharmacology, School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX, England **Bromocriptine and dopamine-receptor stimulation.** Journal of Pharmacy and Pharmacology (London). 28(7):586-588, 1976.

The possibility that bromocriptine, an ergot derivative which produces a marked improvement in a number of clinical conditions, does not act directly in producing its behavioral effect was tested using an animal model in which the nigro/striatal dopaminergic pathway was not destroyed, but its activity was altered by placing small electrolytic lesions in the zona reticulata of the substantia nigra. Data obtained from studying male albino rats indicated a clear difference in the interactions of bromocriptine with apomorphine induced or amphetamine induced rotational behavior and suggest possible complex effects of dopaminergic neurotransmission. That bromocriptine does not induce behavioral changes when brain dopamine is depleted suggests an important involvement of endogenous dopamine. While results do not allow a clearcut distinction regarding the precise mode of action of bromocriptine, its ability to stimulate central dopamine receptors appears to differ from that of apomorphine. 12 references.

001191 Dubois, M.; Scuvée-Moreau, J.; Dresse, A. no address **Recording of the electrophysiological activity of the locus coeruleus in the rat./ Essai d'enregistrement de l'activité électrophysiologique du locus coeruleus du rat.** Neuropsychobiologie (Basel). 2(4):203-210, 1976.

The unitary electrophysiological activity of the noradrenalin containing neurons of the rat locus coeruleus (LC) was recorded. The experimental conditions allowing a reproducible recording of this activity are defined. It was shown that the neurons of the LC slowly discharge, at a frequency of 1-3/sec with an amplitude of 100-150 mV. This spontaneous activity is greatly reduced by low doses of norimipramine, a tricyclic antidepressant. 22 references. (Author abstract modified)

001192 Dubost, M.; Escousse, A.; Mounie, J.; Truchot, R. Laboratory of Medical Pharmacology, University of Dijon,

Dijon, France **Peripheral effects of the amphetamine-type anorectic drugs: inhibition of catecholamine-induced lipolysis, respiration, glucose utilization in the adipose tissue of man and rat.** *British Journal of Pharmacology* (London). 58(3):436P-437P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the inhibition of catecholamine induced lipolysis, respiration, and glucose utilization in the adipose tissue of humans and rats in vitro as a peripheral effect of amphetamine type anorectic drugs. Fenfluramine, fenproporex and chlorphentermine were shown to be weak inhibitors of noradrenaline in both humans and rats while fenproporex and chlorphentermine also depressed cellular respiration. Fenfluramine had no effect on the cellular respiration of rats and increased it in humans.

001193 Dumovic, P.; Burrows, G. D.; Vohra, J.; Davies, B.; Scoggins, B. A. Dept. of Psychiatry, University of Melbourne, Clinical Sciences Bldg., Royal Melbourne Hospital, Parkville, Vic. 3050, Australia **Effect of tricyclic antidepressant drugs on the heart.** *Archives of Toxicology* (Berlin). 35(4):255-262, 1976.

The effects on the heart rate and ECG of anesthetized guinea pigs of amitriptyline, doxepin, imipramine and nortriptyline infused at 1mg/kg/min until death were observed. In addition an in vitro study on guinea-pig atria was performed on the chronotropic and inotropic effects of these drugs and of desmethylinipramine and protriptyline. The effect of sodium bicarbonate and propranolol on amitriptyline and doxepin induced ECG changes was also assessed. A difference in the cardiac effects of the in vivo and in vitro model was observed. Guinea-pigs infused with doxepin survived significantly longer than those infused with amitriptyline, imipramine or nortriptyline. No statistically significant difference was found among the tricyclic drugs with respect to onset of the widening of the QRS complex, increased PR and QT intervals. In the spontaneously beating atrial preparation doxepin was the most potent cardiodepressant. Sodium bicarbonate had no effect on arrhythmias induced by the tricyclics, while propranolol, apart from the bradycardia induced, was without beneficial effect on the ECG. The guinea-pig provides a good model for studying the arrhythmogenic actions of tricyclic antidepressants. 26 references. (Journal abstract)

001194 Dunstan, Robin; Jackson, David M. Department of Pharmacology, University of Sydney, New South Wales 2006, Australia **The demonstration of a change in adrenergic receptor sensitivity in the central nervous system of mice after withdrawal from long-term treatment with haloperidol.** *Psychopharmacology* (Berlin). 48(1):105-114, 1976.

Using locomotor activity as a reproducible behavioral response, the effect of withdrawing mice from long-term haloperidol treatment on their responsiveness to clonidine, apomorphine and dexamphetamine administration was investigated. Locomotor stimulation to clonidine after haloperidol cessation was blocked by FLA-63. Haloperidol treated animals displayed a supersensitive response to dexamphetamine which was blocked by phenoxybenzamine and pimoze. The data suggest that long-term haloperidol treatment leads to the development of supersensitive adrenergic receptors in the central nervous system, which appropriately stimulated, effect an increase in locomotor activity. Moreover, the results indicate that a large component of the supersensitive response to dexamphetamine observed after long-term haloperidol treatment is due to adrenergic receptor supersensitivity. However, the dopamine receptor (which was shown to be supersensitive to apomorphine) is of fundamental im-

portance because phenoxybenzamine and phentolamine, while blocking the supersensitive response to dexamphetamine, failed to block the response to dexamphetamine in vehicle treated animals, which was, however, blocked by pimoze. 44 references. (Author abstract modified)

001195 Eibergen, Robert D.; Carlson, Kristin R. Box 3838, Duke University Medical Center, Durham, NC 27710 **Behavioral evidence for dopaminergic supersensitivity following chronic treatment with methadone or chlorpromazine in the guinea pig.** *Psychopharmacology* (Berlin). 48(2):139-146, 1976.

The effects of chronic treatment with methadone or chlorpromazine on two behaviors (amphetamine induced stereotyped oral behaviors and open-field locomotion) which are thought to depend primarily on the striatal dopamine system were studied in guinea pigs. Following a 5-week treatment with methadone (MD), chlorpromazine (CPZ), or saline, the dopamine agonist methamphetamine (MA) elicited more intense stereotypies in the MD and CPZ animals. After chronic treatment with MD, the MA elicited stereotypies were reduced by an acute dose of MD. Stereotyped oral behaviors elicited by a stressful stimulus (footshock) were enhanced in the MD animals both during and following chronic drug treatment. MA elicited open field locomotion, measured 2 weeks following termination of chronic drug treatment, was enhanced in the MD and CPZ animals. It is suggested that chronic treatment with MD or CPZ produces a prolonged dopaminergic supersensitivity which may be especially relevant to patients in methadone maintenance programs. 38 references. (Author abstract modified)

001196 Emson, P. C. MRC Neurochemical Pharmacology Unit, University Dept. of Pharmacology, Hills Road, Cambridge, England **Effects of chronic treatment with amino-ox-yacetic acid or sodium n-dipropylacetate on brain GABA levels and the development and regression of cobalt epileptic foci in rats.** *Journal of Neurochemistry* (Oxford). 27(6):1489-1494, 1976.

The effects of acute and chronic administration of amino-ox-yacetic acid (AOAA) and n-dipropylacetate (DPA) on the cobalt epileptic focus and brain gamma-aminobutyric acid (GABA) levels were investigated in rats through monitoring of electrocorticogram data and bioassay techniques. Results reveal that AOAA acute treatment caused epileptic spike suppression within 30 to 90 minutes. In contrast, DPA acute treatment had no effect on spike frequency. Chronic treatment of cobalt epileptic rats with AOAA or with DPA elevated brain GABA concentrations significantly and reduced brain glutamate decarboxylase activity relative to saline controls. Brain gamma-aminobutyrate aminotransferase activity was significantly reduced by chronic AOAA treatment, but chronic DPA treatment had no effect. Chronic AOAA treatment reduced the frequency of epileptic spikes at secondary foci, most markedly at doses of 5mg/kg/day. Chronic DPA administration had no long-term anticonvulsant activity. It is concluded that the anticonvulsant action of DPA and, most likely, AOAA is not mediated by a mechanism involving elevation of brain GABA. 22 references. (Author abstract modified)

001197 Estler, C.-J.; Fulle, P. Pharmakologisches Institut, Universität Erlangen-Nürnberg, Universitätsstrasse 22, D-8520 Erlangen, Germany **Effects of antagonists of adrenaline receptors and dopamine receptors on morphine-stimulated glycogen breakdown in mouse brain.** *Journal of Neurochemistry* (Oxford). 27(2):629-630, 1976.

The effects of antagonists of adrenaline receptors and dopamine receptors on morphine stimulated glycogen breakdown in mouse brain were studied in order to indicate whether adrenaline receptors or dopamine receptors mediate the effect. Experimental mice were injected intraperitoneally before subcutaneous administration of morphine, and animals were killed and dissected for use in enzymic determination of glycogen. Morphine caused a rapid decline of the cerebral glycogen content in mice. Propranolol increased cerebral glycogen content, but did not diminish the glycogenolytic effect of morphine. Phenoxybenzamine alone produced a dose dependent lowering of glycogen content, and completely inhibited the glycogenolytic action of morphine. Phentolamine alone had no significant effect on brain glycogen, but greatly reduced the glycogenolytic effect of morphine. Pimozide by itself did not significantly affect the glycogen content, but inhibited the morphine produced reduction of the glycogen content. Metoclopramide did not affect the action of morphine on brain glycogen. Interpretation of results relating to the mode of action of morphine is complicated by the fact that glycogen breakdown was inhibited by two different kinds of antagonists and that the specificity of the antagonists is limited. It is tentatively concluded that alpha-adrenoreceptors are most essential for the glycogenolytic action of morphine. 11 references.

001198 Ettenberg, Aaron; Wise, Roy A. Center for Research on Drug Dependence, Department of Psychology, Concordia University, Montreal, Canada **Non-selective enhancement of locus coeruleus and substantia nigra self-stimulation after termination of chronic dopaminergic receptor blockade with pimozide in rats.** *Psychopharmacology Communications*. 2(2):117-124, 1976.

The effects of release from chronic dopaminergic receptor blockade on nonrepinephrine (NE) and dopamine (DA) self-stimulation were studied in rats. Self-stimulation of substantia nigra and locus coeruleus were assessed before and after 8 days of pimozide administration. Self-stimulation was increased in both sites 48 hours after termination of pimozide. It is suggested that pimozide induces supersensitivity in a dopaminergic substrate. This substrate appears to be critical for intracranial self-stimulation even when its fibers are not directly activated by the stimulating electrode. 12 references. (Author abstract modified)

001199 Evans, Richard Henry; Francis, Alison Anne; Watkins, Jeffrey Clifton. Department of Pharmacology, Medical School, Bristol BS8 1TD, England **Bimodal action of glycine on frog spinal motoneurons.** *Brain Research (Amsterdam)*. 118(3):395-401, 1976.

The bimodal action of glycine on frog spinal motoneurons was investigated as a continuation of studies showing that in the presence of procaine the changes in electrical potential caused by glycine in the ventral root of the isolated hemisectioned spinal cord of the frog were compounded of both hyperpolarizing and depolarizing responses to the amino acid. From a comparison of effects of changes in perfusion medium on potentials produced by glycine, beta-alanine, and L-glutamate in the presence and absence of strychnine, it was concluded that glycine acts on a similar receptor to beta-alanine and causes a hyperpolarizing response which is blocked by strychnine. However, the glycine has an additional, depolarizing, action which is usually the major effect and masks the hyperpolarizing response. The depolarizations produced by L-glutamate and glycine could be differentiated by their different ionic dependencies. The glycine depolarization was selectively decreased by a lowered sodium ion concentration in the medi-

um while L-glutamate depolarizations were selectively enhanced by lowered potassium ion concentration. 11 references. (Author abstract modified)

001200 Farska, I.; Krulik, R. Psychiatric Research Unit, Faculty of Medicine, Charles University, Prague 2, Ke Karlovu II, Czechoslovakia **Psychotropic drugs and metabolic enzymes in rat brain.** *Journal of Neurochemistry (Oxford)*. 27(5):1283-1284, 1976.

The effects of chlorpromazine, amitriptyline and chlordiazepoxide on the activities of energy metabolic enzymes were studied in vitro in rat brain homogenates, the crude mitochondrial fraction, and the nerve ending fraction. Adenylate kinase and 5'-nucleotidase in rat brain homogenate were not significantly affected by any of the drugs. The other enzymes studied, (magnesium adenosine triphosphatase (Mg-ATPase), sodium potassium adenosine triphosphatase (Na-K-ATPase), calcium adenosine triphosphatase (Ca-ATPase), deoxyribonucleotide phosphate adenosine triphosphatase (DNP-ATPase), and creatine kinase were inhibited by chlorpromazine and amitriptyline but not by chlordiazepoxide. Chlorpromazine and amitriptyline inhibited Mg-ATPase, Na-K-ATPase and creatine kinase activity in the synaptosomes more than in the crude mitochondrial fraction. Chlorpromazine inhibited Ca-ATPase activity more in the crude mitochondrial fraction than in the synaptosomes and inhibited DNP-ATPase activity in the crude mitochondrial fraction more than did amitriptyline. It is concluded that psychotropic drugs do not interfere with nucleotide metabolism equally at all levels. 15 references.

001201 Fillion, G.; Fillion, M. P.; Jacob, J.; Rousselle, J. C. Department of Pharmacology, Pasteur Institute, Paris, France **5-HT and LSD high affinity binding sites to brain synaptosomal membranes.** *British Journal of Pharmacology (London)*. 58(3):425P-426P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the binding of 5-hydroxytryptamine (5-HT) and lysergic acid diethylamide (LSD) to various sites of bovine brain synaptosomal membranes. Membranes incubated with tritiated 5-HT and LSD shows that both drugs apparently have a saturable, reversible, high affinity binding, with LSD having a second saturable and reversible site of less affinity not shared by 5-HT. Regional distributions of binding capacities for LSD and 5-HT were shown to be very similar but not homogenous within the brain. These studies seem to indicate that the different sites observed correspond to an agonist and an antagonist conformation of the same 5-HT receptor site. 1 reference.

001202 Fink, Steve A.; Williams, John A. Dept. of Physiology, University of California, San Francisco, CA 94143 **Adrenergic receptors mediating depolarization in brown adipose tissue.** *American Journal of Physiology*. 231(3):700-706, 1976.

Adrenergic receptors mediating depolarization in vitro neonatal rat brown adipose tissue (BAT) have been characterized by use of adrenergic agonists and antagonists. Releasable endogenous catecholamine was present in BAT as demonstrated by tyramine induced and 1,1-dimethyl-4-phenylpiperazinium iodide (DMPP) induced depolarization in BAT from normal rats and its absence when BAT from reserpinized rats was used. In BAT from reserpinized rats l-norepinephrine, l-phenylephrine, and l-isoproterenol all similarly depolarized the brown adipocytes. Dopamine and d-norepinephrine were more than 100 times less potent. The beta-adrenergic blocker propranolol competitively inhibited isoproterenol induced depolarization, whereas the alpha-adrenergic blockers, phen-

tolamine and phenoxybenzamine, inhibited the phenylephrine induced depolarization with much smaller inhibitory effects on the isoproterenol induced depolarization. Both the agonist and antagonist studies are interpreted as indicating the presence of both alpha and beta-adrenergic receptors on BAT cells which mediate catecholamine induced depolarization. 40 references. (Author abstract modified)

001203 Fludder, Joan M.; Tonge, Sally R. School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool, L3 3AF, England **Modification by oestrogen of the effects of (d)-amphetamine sulphate on noradrenaline metabolism in discrete areas of rat brain.** British Journal of Pharmacology (London). 58(3):422P-423P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the modification by estrogen of the effects of d-amphetamine sulfate on noradrenaline metabolism in the midbrain and amygdala of the rat. Noradrenaline depletion in ovariectomized animals was accelerated by ethinylestradiol following amphetamine administration. Noradrenaline depletion after 4, alpha-dimethyl-m-tyrosine (which reflects changes in noradrenaline neuronal uptake mechanisms) was antagonized in the amygdala, but not in the midbrain, by ethinylestradiol. It is suggested that the effects are, to some extent, dependent on the relative preponderance of noradrenaline terminals or noradrenaline axonal bodies in each brain area, and that noradrenaline metabolism cannot be treated as a single homogenous system in the central nervous system. It is also suggested that both amphetamine and estrogens release noradrenaline -- amphetamine by stimulating release from catecholamine terminals while inhibiting impulse flow, and estrogens by stimulating total turnover of noradrenaline.

001204 Fludder, Joan; Tonge, Sally. Polytechnic, Byrom Street, Liverpool L3 3AF, England **Interaction between amphetamine and progesterone: effects on noradrenaline metabolism in discrete areas of rat brain.** Journal of Pharmacy and Pharmacology (London). 28(Supplement):35P, 1976.

The interaction between amphetamine and progesterone and their effects on norepinephrine metabolism in the rat brain are discussed. Progesterone increased normetanephrine levels in the midbrain and amygdala without affecting norepinephrine levels, while (+)-amphetamine reduced norepinephrine levels in both brain areas and increased normetanephrine levels in the amygdala. Normetanephrine and norepinephrine levels were higher in the amygdala and lower in the midbrain regions of ovariectomized than of intact rats. Progesterone reduced amygdaloid norepinephrine but increased midbrain norepinephrine and amygdaloid and midbrain normetanephrine levels in ovariectomized rats. Amphetamine alone was without effect, but in combination with progesterone reduced amygdaloid normetanephrine concentrations. Norepinephrine turnover was slower in ovariectomized than in diestrous rats, and was further retarded by progesterone. Progesterone antagonized depletion of norepinephrine by 4, alpha-dimethyl-m-tyramine. It is suggested that amphetamine and progesterone produce their individual effects through different cellular processes and that progesterone may prevent the uptake of amphetamine by neuronal and/or storage granule membranes without antagonizing the depression of synthesis activity. 8 references.

001205 Fog, Rasmus, Pakkenberg, H.; Juul, Per; Bock, Elisabeth; Jorgensen, O. S.; Andersen, John. Psychopharmacological Laboratory, St. Hans Hospital, Dept. E, DK-4000 Roskilde, Denmark **High-dose treatment of rats with**

perphenazine enanthate. Psychopharmacology (Berlin). 50(3):305-307, 1976.

The effects of high doses of perphenazine enanthate on the basal ganglia and cortex of rats were examined. A treatment period of 6 months and a dose of perphenazine enanthate of 40mg/kg s.c. every 2nd week was used. No significant differences from control animals were found by cell counting in the basal ganglia and the cortex, by electron microscopy investigation of the same structures, or by quantitative immunoelectrophoresis of proteins from the corpus striatum and the cortex. The uptake of 3H-uridine measured by autoradiography in the cortex and in the liver was, however, 20-50% higher in the experimental group. The influences of dose level, duration of treatment period, and animal age are discussed and correlated to the clinical syndrome of tardive dyskinesia seen in patients treated with neuroleptic drugs. 7 references. (Author abstract)

001206 Forney, Ellen; Klemm, W. R. Department of Biology, Texas A&M University, College Station, TX 77843 **Effect of ethanol on impulse activity in isolated cerebellum.** Research Communications in Chemical Pathology and Pharmacology. 15(4):801-804, 1976.

An investigation was carried out to determine whether the effects of ethanol on the cerebellum of rats are direct or indirect (mediated via neural pathways from other brain structures). After denervation of the cerebellum by large electrolytic lesions of the peduncles, intraperitoneal injection of ethanol generally depressed impulse activity of neuronal populations in the cerebellar cortex. In saline treated controls, the impulse activity was increased. It is concluded that moderate doses of ethanol have a direct, suppressive action on cerebellar neurons. 8 references. (Author abstract modified)

001207 Fozard, J. R.; Berry, J. L. University of Manchester, Oxford Road, Manchester M13 9PT, England **Interactions between antimigraine drugs and a high affinity uptake and storage mechanism for 5-hydroxytryptamine.** Pharmacology (Basel). 14(4):357-361, 1976.

The effects on the uptake of two antimigraine drugs, ergotamine and methysergide, were studied in the isolated rabbit heart in relation to the migraine syndrome where plasma 5-hydroxytryptamine (5-HT) concentrations drop sharply at the onset of an attack and remain low while the headache persists. Ergotamine tartrate caused a small increase in H-5HT uptake by the heart. Methysergide bimeleate slowed the appearance of metabolites in the perfusion fluid. Because of the high concentrations required, neither observation seems likely to be of clinical significance to migraine. It is concluded that the frequently observed sensitization of tissues to 5-HT by ergotamine and methysergide is not the result of inhibition of its tissue uptake. 11 references. (Author abstract modified)

001208 Frederickson, Robert C. A.; Hewes, Christina R.; Aiken, James W. Division of Pharmacological Research, Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN. **Correlation between the in vivo and an in vitro expression of opiate withdrawal precipitated by naloxone: their antagonism by lambda(-)-delta-9-tetrahydrocannabinol.** Journal of Pharmacology and Experimental Therapeutics. 199(2):375-84, 1976.

The in vivo and in vitro antagonism of naloxone precipitated morphine withdrawal symptoms in guinea pigs by lambda(-)-delta-9-tetrahydrocannabinol (THC) was studied. Treatment of morphine dependent guinea pigs in vivo and ileum segments from dependent animals in vitro with THC inhibits withdrawal

symptoms produced by injection of naloxone. Both the in vivo and in vitro responses were specific for the opiate dependent state and were dependent on naloxone dose, with time courses of the development and decline of the two responses being similar. THC produced a stereospecific, dose dependent inhibition of naloxone precipitated withdrawal in guinea pigs and rats that was more complete than and different from that produced by sedatives. THC also antagonized the naloxone effect on the ileum without affecting responses to acetylcholine. This action on dependent ileum seems to be via reduction in acetylcholine, and while the action of THC may not be exactly the same, it serves as a possible model for the mechanism of action. Results also suggest that cannabinoids may be useful in opiate detoxification. 26 references. (Author abstract modified)

001209 Frederickson, Robert C. A.; Norris, Franklin H. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Enkephalin-induced depression of single neurons in brain areas with opiate receptors -- antagonism by naloxone.** Science. 194(4263):440-442, 1976.

Enkephalin and morphine was applied microiontophoretically to single neurons in various brain areas in rats to determine its effects. Enkephalin was found to depress spontaneous and glutamate induced firing of single neurons in frontal cortex, caudate nucleus, and periaqueductal gray matter, where enkephalin and high concentrations of opiate receptors are found. Many of the depressions were blocked by the specific narcotic antagonist naloxone hydrochloride. The data are compatible with a neurotransmitter or neuromodulator role for this new brain pentapeptide. 33 references. (Author abstract)

001210 Freye, E.; Kuschinsky, K. Max-Planck-Institut für experimentelle Medizin, D-3400 Göttingen, Germany **Effects of fentanyl and droperidol on the dopamine metabolism of the rat striatum.** Pharmacology (Basel). 14(1):1-7, 1976.

A study was carried out in rats to: 1) examine the effects of fentanyl on dopamine (DA) metabolism in the striatum; 2) determine whether naloxone reverses these effects; 3) compare the effect of fentanyl with that of droperidol; and 4) compare the effect of droperidol on DA turnover with that of haloperidol. Fentanyl in low doses had no significant effect on DA turnover 20 min after intraperitoneal (i.p.) injection and raised the homovanillic acid (HVA) concentration in the rat striatum. The maximum effect occurred 60 min after injection. Higher doses reduced the HVA content after 20 min and raised it after 60 min. Naloxone given shortly after high doses of fentanyl eliminated the early decrease and the late increase of HVA content in the striatum. Naloxone alone slightly increased the HVA concentration. Droperidol and haloperidol markedly increased the HVA content in the rat striatum 90 min after injection. These effects were dose dependent. Naloxone did not significantly inhibit the rise of HVA induced by droperidol. 18 references. (Author abstract modified)

001211 Friedman, E.; Shopsin, B.; Gershon, S. New York University Medical Center, 550 First Avenue, New York, NY 10016 **Effects of tranylcypromine on 5-HT uptake and its interaction with PCPA on rat brain 5-HT.** Research Communications in Chemical Pathology and Pharmacology. 15(1):191-194, 1976.

The effect of p-chlorophenylalanine (PCPA) treatment in rats receiving chronic treatment with tranylcypromine on brain serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) levels was examined. This treatment schedule was similar to that followed in depressed patients undergoing treatment with the monoamine oxidase inhibitor. PCPA completely obviated

the elevation in serotonin and further reduced 5-HIAA levels of animals treated chronically with tranylcypromine. These effects correlated with PCPA induced reversal in the clinical improvement achieved by tranylcypromine. In vitro studies, tranylcypromine was found to inhibit 5-HT uptake into synaptosomes with a minimal action on the spontaneous release of the amine. It is concluded that the alteration in 5-HT is involved in the antidepressant effect of tranylcypromine. 6 references. (Author abstract modified)

001212 Friedman, Marvin A. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Inhibition of arylhydrocarbon hydroxylase induction in BALB/C mouse liver by delta9-tetrahydrocannabinol.** Research Communications in Chemical Pathology and Pharmacology. 15(3):541-552, 1976.

The effects of delta9-tetrahydrocannabinol (delta9-THC) on the induction of arylhydrocarbon hydroxylase activity by phenobarbital and 3-methylcholanthrene were determined in male BALB/C mice. Phenobarbital induced the enzyme activity of arylhydrocarbon hydroxylase by 164%, and delta9-THC completely abolished this enzyme induction. Phenobarbital induced the enzyme activity of aminopyrine demethylase by 74%, and delta9-THC reduced this enzyme induction to 43%. Treatment with 3-methylcholanthrene induced arylhydrocarbon hydroxylase to 455% of control, while the group treated with both 3-methylcholanthrene and delta9-THC was induced to only 177% of its control. The delta-9-THC treated mice showed inactivity, appetite suppression, and weight loss. These drugs do not appear to have any interactive effect on microsomal protein synthesis, but are potent antagonists in the synthesis of nuclear RNA. 15 references. (Author abstract modified)

001213 Fuentes, Jose. Section of Pharmacology, Institute of Medical Chemistry, C.S.I.C., Madrid 6, Spain **Inhibition of 2-phenylethylamine metabolism in brain by type B monoamine oxidase blockers.** (Unpublished paper). SMRP-IR-MH, NIMH, 1976.

The biological mechanisms and clinical aspects of the interaction between 2-phenylethylamine (PEA) and monoamine oxidase (MAO) are reviewed. Among the topics discussed are: 1) MAO and the metabolism of PEA; 2) multiple forms of MAO; 3) specific MAO substrates and MAO inhibitors; 4) distribution of type A MAO and type B MAO in the brain; 5) the use of selective MAO inhibitors to evaluate functions modulated by the various enzymes; 6) the mechanism by which MAO inhibitors produce their antidepressant effects (blockade of MAO or blockade of amine reuptake); and 7) the effect of specific inhibitors on reserpine sedation in the rat. 28 references.

001214 Fulginiti, Susana; Molina, Victor A.; Orsingher, Otto A. Departamento de Farmacologia, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Estafeta 32, Córdoba, Argentina **Inhibition of catecholamine biosynthesis and memory processes.** Psychopharmacology (Berlin). 51(1):65-69, 1976.

The effects of inhibition of catecholamine biosynthesis by injections of the dopamine beta-hydroxylase inhibitor diethyldithiocarbamate (DDC) or the tyrosine hydroxylase inhibitor alpha-methyl tyrosine (alpha-MT) on retention of conditioned avoidance responses (CAR) were examined in rats. Injections of alpha-MT immediately after training impaired retention of the CAR. DL-DOPA, which restores brain catecholamine levels in alpha-MT treated animals, counteracted the effects of

alpha-MT if administered within 2 hr after the alpha-MT but not if administered more than 2 hr later. Posttrial injections of 600mg/kg of DDC, but not 300mg/kg, impaired retention of CAR. Administration of alpha-MT immediately after passive avoidance training reduced memory in females but not in males. It is suggested that memory consolidation processes require the presence of noradrenaline for about 2 hr after training. 32 references. (Author abstract modified)

001215 Fulton, Stephanie C.; Healy, M. D. Incarnate Word College of the United Colleges of San Antonio, San Antonio, TX 78209 **Comparison of the effectiveness of deserpidine, reserpine, and alpha-methyltyrosine on brain biogenic amines.** Federation Proceedings. 35(14):2558-2562, 1976.

The comparative effects of reserpine and deserpidine, alone and in combination with alpha-methyltyrosine (AMT) on depletion of dopamine (DA), norepinephrine (NE) and serotonin (5-hydroxytryptamine, 5-HT) from their storage pools in rat brains were investigated. Reserpine and deserpidine were equally potent in reducing the concentrations of the three biogenic amines (to about 50% of control values) when used alone. Deserpidine plus AMT produced a greater reduction in the amine levels than did reserpine plus AMT. It is pointed out that AMT, alone and in combination with either alkaloid, reduced 5-HT levels as well as those of DA and NE. 31 references.

001216 Furuta, Yasuhiko; Yoshikawa, Akira. Research Laboratories, Nippon Kayaku Co., Shimo, Kita-ku, Tokyo 115, Japan **Reversible adrenergic alpha-receptor blocking action of 2,4'-dimethyl-3-piperidino-propiofenone (tolperisone).** Japanese Journal of Pharmacology (Kyoto). 26(5):543-550, 1976.

The vascular action of 2,4'-dimethyl-3-piperidino-propiofenone hydrochloride (tolperisone hydrochloride), a centrally acting muscle relaxant, was investigated in pentobarbital anesthetized dogs. Tolperisone given intravenously produced a transient hypotension, tachycardia, and hyperventilation. The drug increased the femoral arterial flow, and decreased the superior mesenteric arterial flow following an initial transient increase. When injected directly into femoral and mesenteric arteries, tolperisone caused a rapid increase in both arterial flows (vasodilatation). However, femoral vessels were about 90 times as sensitive as mesenteric vessels to tolperisone. These results indicate that tolperisone shifts the blood volume from mesenteric (visceral) vessels to femoral (skeletal) ones. The femoral vasodilatation produced by intraarterial tolperisone was not depressed by the pretreatment with intraarterial propranolol, atropine, or chlorphenylamine. Tolperisone decreased the contractile force in an isolated and cross circulated papillary muscle. Tolperisone produced adrenaline reversal and antagonized the pressor response to noradrenaline. Moreover, femoral vasoconstriction caused by intraarterial adrenaline was converted to vasodilatation and that caused by intraarterial noradrenaline was depressed during an intraarterial infusion of tolperisone. These results indicate that tolperisone blocks adrenergic alpha-receptors. The blocking action was rapid in onset, short-lived, and in addition, competitive. 6 references. (Author abstract)

001217 Gal, J.; Wright, J.; Cho, A. K. Department of Pharmacology, School of Medicine, University of California at Los Angeles, Los Angeles, CA 90024 **In vitro metabolism of amphetamine: an apparent enantiomeric interaction.** Research Communications in Chemical Pathology and Pharmacology. 15(3):525-540, 1976.

The in vitro metabolism of (R)-amphetamine and (S)-amphetamine was studied using livers from male New Zealand white rabbits. The major metabolites formed were N-hydroxy-yamphetamine and 1-phenyl-2-propanol. Small amounts of phenylacetone oxime were also found. When (R)-amphetamine and (S)-amphetamine were incubated separately, (R)-amphetamine was metabolized more rapidly. However, in incubations of racemic substrate, (S)-amphetamine was metabolized more rapidly, suggesting that (S)-amphetamine or one of its metabolites inhibits the metabolism of (R)-amphetamine. 16 references.

001218 Gehrmann, John E.; Killam, Keith F., Jr. Department of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **Assessment of CNS drug activity in rhesus monkeys by analysis of the EEG.** Federation Proceedings. 35(11):2258-2263, 1976.

The effects of drugs with a wide range of central nervous system (CNS) activities on neocortical EEGs of Macaca mulatta monkeys were examined according to the specificity of autospectral changes at different anatomical sites. Changes in total spectral power, in the shape of the spectral envelope, and in the relative stability of the drug induced EEG were assessed at various doses. Electroencephalograms were recorded from epidural electrodes under resting conditions and under the influence of CNS drugs, (amobarbital, clorazepate, glutethimide, codeine, naloxone, naltrexone, morpaine, nalbuphine, chlorpromazine, amitriptyline, diazepam). Autospectra representing sequential four second samples of EEG were generated successively over a nominal frequency band of 0-64Hz. Averages of sequential autospectra were computed over specified time periods. Spectral power over the entire bandwidth and selected frequency regions was calculated and compared. This facilitated the grouping of drugs with similar activities, as well as the distinguishing of changes not readily detectable by visual inspection of the conventional EEG in the time domain. 21 references. (Author abstract modified)

001219 Geller, Herbert M. Department of Pharmacology, C.M.D.N.J.-Rutgers Medical School, Piscataway, NJ 08854 **Effects of some putative neurotransmitters on unit activity of tuberal hypothalamic neurons in vitro.** Brain Research (Amsterdam). 108(2):423-430, 1976.

A study was carried out using explant tissue cultures of rat brain arcuate nucleus and median eminence to investigate the direct effects of putative neurotransmitters on tuberal neuronal activity in the absence of normal afferents and cyclic hormonal fluctuations. Slowly firing cells were excited with iontophoretic D, L-homocysteic acid (DLH) or glutamate. Direct application of the monoamine neurotransmitters norepinephrine, dopamine and serotonin depressed the overwhelming majority of neurons on which they had an effect. Iontophoretic application of acetylcholine affected a minority of cells to which it was applied; effects were about evenly divided between excitation and inhibition. Locally applied histamine produced an excitatory effect in approximately half of the cells to which it was applied. Gamma-aminobutyric acid (GABA) and glycine were inhibitory. It is concluded that pharmacological diversity of the tuberal area of the hypothalamus is reflected in responses of neurons in the explant cultures. 33 references.

001220 Gianutsos, Gerald; Thornburg, John E.; Moore, Kenneth E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Differential actions of dopamine agonists and antagonists on the gamma-butyrolactone-induced**

increase in mouse brain dopamine. *Psychopharmacology* (Berlin). 50(3):225-229, 1976.

The differential actions of dopamine agonists and antagonists on the gamma-butyrolactone (GBL) induced increase in mouse brain dopamine were examined. Apomorphine dose dependently antagonized the GBL effect, while piribedil was less effective. Haloperidol prevented the antagonism of GBL by apomorphine but pimozide was ineffective in blocking apomorphine. After chronic treatment with haloperidol or pimozide, there was no alteration of the maximum GBL induced increase in dopamine nor was there any significant change in the antagonism by apomorphine, although a trend toward increased sensitivity to apomorphine was noted in the group withdrawn from haloperidol. The results suggest that in the mouse, haloperidol is a more effective antagonist of presynaptic dopamine autoreceptors than pimozide, while apomorphine is a better presynaptic agonist than piribedil. 18 references. (Author abstract)

001221 Giovine, A.; Renis, M.; Bertolino, A. Mental Hospital 'Casa Divina Provvidenza', I-70052 Bisceglie, Italy *In vivo* and *in vitro* studies on the effect of tetrahydropapaveroline and salsolinol on COMT and MAO activity in rat brain. *Pharmacology* (Basel). 14(1):86-94, 1976.

Studies were made of the effect of tetrahydropapaveroline (THP) on catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO) activity *in vivo* in the rat brain and of THP and salsolinol methylation capacity *in vitro*. Both alkaloids use COMT enzymes for methylation and can act as competitive inhibitors of COMT activity and MAO activity. 31 references. (Author abstract modified).

001222 Gomes, Benedict; Kloepper, Hans G.; Oi, Susumu; Yasunobu, Kerry T. Dept. of Biochemistry-Biophysics, University of Hawaii School of Medicine, Honolulu, HI 96822 *The reaction of sulfhydryl reagents with bovine hepatic monoamine oxidase: evidence for the presence of two cysteine residues essential for activity.* *Biochimica et Biophysica Acta* (Amsterdam). 438:347-357, 1976.

In order to further investigate the effect of sulfhydryl reagents on purified bovine hepatic monoamine oxidase, the protective actions of substrate and competitive inhibitors on inactivation of the enzyme, and the kinetics of the reactions involved, a series of experiments were undertaken. It was found that bovine liver monoamine oxidase (EC 1.4.3.4) was found to be inactivated by various well known sulfhydryl reagents like p-mercuribenzoate, methylmercuric iodide and 5,5'-dithiobis(2-nitro benzoic acid), and that the inactivation of the enzyme results from reactions of these reagents with 2 out of 8 titratable sulfhydryl groups per 10 to the fifth g of the enzyme. The substrate, benzylamine, and competitive inhibitors like benzaldehyde, p-nitrobenzaldehyde, benzyl alcohol protected the enzyme from inactivation by the mercurials or the Ellman reagent. The inactivation experiments with these sulfhydryl reagents, the protection experiments, and the kinetics as well as physicochemical observations suggest that there are only two cysteine residues that are required for activity of the enzyme. It is possible that the two residues may be active center residues. 17 references. (Author abstract modified)

001223 Gomes, C.; Svensson, T. H.; Trolin, G. Departments of Biochemistry and Pharmacology, Escola Paulista de Medicina, S. Paulo, Brasil *Effects of morphine on central catecholamine turnover, blood pressure and heart rate in the rat.* *Naunyn-Schmiedeberg's Archives of Pharmacology* (Berlin). 294(2):141-147, 1976.

The relationship between the effects of morphine on central catecholamine (CA) turnover and the effects of the drug on cardiovascular function were investigated in the unanesthetized rat and in the anesthetized rat. In conscious animals morphine caused increased dopamine (DA) turnover, unchanged or increased central noradrenaline (NA) turnover, hypertension and tachycardia. In anesthetized animals, brain DA was not affected, NA turnover was decelerated, particularly in cerebral cortex and medulla oblongata, and hypotension and bradycardia occurred. Biochemical and cardiovascular effects were both antagonized by naloxone. Decerebration just inferior to the inferior colliculus abolished the cardiovascular effects of morphine in conscious rats. It is suggested that: 1) morphine induced cardiovascular effects are related to or mediated by the effects of the drug on brain NA mechanisms; 2) the higher brain structures appear important in the excitatory effects of morphine, while structures below the decerebration level, such as the medulla oblongata, appear primarily involved in the hypotension and bradycardia obtained in anesthetized animals; and 3) morphine may have a biphasic dose response curve with respect to cardiovascular function and, by inference, on brain NA mechanisms. 37 references. (Author abstract modified)

001224 Goodale, David B.; Moore, Kenneth E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 *A comparison of the effects of decarboxylase inhibitors on L-dopa-induced circling behavior and the conversion of dopa to dopamine in the brain.* *Life Sciences* (Oxford). 19(5):701-706, 1976.

The conversion in the brain of intravenously administered 3H-dopa to 3H-dopamine was determined in mice at various times after the administration of several inhibitors of aromatic L-amino acid decarboxylase. The effects of these same decarboxylase inhibitors were determined on the L-dopa induced circling in mice with unilateral 6-hydroxydopamine lesions of striatum. L-Dopa induced contralateral circling is correlated temporally with the conversion of this amino acid to dopamine in the brain. The specific inhibitor administered and the pretreatment interval time chosen are critical factors to consider when inhibitors of cerebral decarboxylase are being employed. 12 references. (Author abstract modified)

001225 Govoni, S.; Fresia, P.; Spano, P. F.; Trabucchi, M. Department of Pharmacology and Therapeutics, University of Brescia, Italy *Effect of desmethyldiazepam and chlordesmethyldiazepam on 3',5'-cyclic guanosine monophosphate levels in rat cerebellum.* *Psychopharmacology* (Berlin). 50(3):241-244, 1976.

The effects of desmethyldiazepam, chlordesmethyldiazepam, and diazepam on 3',5'-cyclic guanosine monophosphate (cGMP) levels in rat cerebellum were examined. Desmethyldiazepam and chlordesmethyldiazepam were several fold more potent than diazepam in decreasing rat cyclic cGMP cerebellar concentrations. None of the three drugs induced detectable changes of cerebellar cyclic 3',5'-adenosine monophosphate (cAMP). On the other hand, the three compounds did not modify the levels of cGMP in cerebellum of newborn rats, where Purkinje cell and dendrites lack synaptic contacts. However, injection of gamma aminobutyric acid (GABA) in the newborn was still able, as in the adult, to decrease cGMP concentration in cerebellum. The data support the hypothesis that cGMP cerebellar concentrations may be a reliable biochemical marker of the clinical activity of benzodiazepines. 19 references. (Author abstract modified)

001226 Green, A. R.; Heal, D. J.; Grahame-Smith, D. G.; Kelly, P. H. MRC Unit and University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England The contrasting actions of TRH and cycloheximide in altering the effects of centrally acting drugs: evidence for the non-involvement of dopamine sensitive adenylate cyclase. *Neuropharmacology* (Oxford). 15(10):591-599, 1976.

The effects of thyrotropin releasing hormone (TRH) and cycloheximide in altering the behavioral responses which follow procedures increasing 5-hydroxytryptamine (5-HT) or dopamine (DA) in the brain and the altering effects of various centrally acting drugs were investigated in rats. The two drugs had opposite effects on monoamine oxidase inhibitor induced locomotor activity, time before onset of pentylenetetrazol induced convulsions, pentobarbital induced sleeping time, and methamphetamine induced locomotor activity. Adenylate cyclase activity and the response of the enzyme to DA were unaltered in the caudate nucleus of animals pretreated by either drug. Neither drug affected circling behavior induced by unilateral nigrostriatal lesioning with apomorphine or apomorphine induced locomotor activity. TRH did not alter brain DA levels or noradrenaline (NA) concentrations; cycloheximide did not alter brain NA concentration but increased the concentration of DA in the brain. Turnover studies indicated that TRH decreased DA synthesis while cycloheximide increased DA synthesis. It is suggested that: 1) neither drug acts by altering postsynaptic dopamine receptor sensitivity; 2) cycloheximide inhibits DA release while TRH may enhance DA release; and 3) the effects of DA release may be the mechanism by which the drugs produce some of their behavioral effects and may explain why TRH appears to have an amphetamine like action. While the drugs appear to act in contrasting ways, it has not been demonstrated that they act at the same site in the brain. 34 references. (Author abstract modified)

001227 Green, Jack P.; Glick, Stanley D.; Crane, Alison M.; Szilagyi, Peter I. A. Department of Pharmacology, Mount Sinai School of Medicine of the City University of New York, New York, NY 10029 Acute effects of morphine on regional brain levels of acetylcholine in mice and rats. *European Journal of Pharmacology* (Amsterdam). 39(1):91-99, 1976.

The effects of acute administration of various doses of morphine on acetylcholine levels, dopamine levels and norepinephrine levels were studied in rats and mice. Morphine increased levels of acetylcholine in mouse striatum in a dose dependent manner, the increase occurring at the lowest dose previously found to produce analgesia and coinciding with the time of peak analgesic effect. Naloxone blocked this increase. After repeated injections of high doses of morphine, no effect was seen. The hippocampus was the only other brain region showing an effect, and this after a high dose. In the rat, morphine increased striatal acetylcholine levels. The ratios in the striatum of levels of acetylcholine to levels of dopamine were significantly increased. Only at the highest dose did morphine increase the levels of dopamine in the striatum and of acetylcholine in the hippocampus. Morphine did not change the levels of norepinephrine in either the hypothalamus or cortex of the rat. 58 references. (Author abstract modified)

001228 Greengrass, P. M.; Waldmeier, P. C.; Imhof, P. R.; Maitre, L. Research Department, Pharmaceuticals Division, CIBA-GEIGY Limited, Basel, Switzerland Comparison of the effects of maprotiline (Ludiomil R) and clomipramine (Anafranil R) on serotonin uptake and tryptophan-binding in plasma. *Biological Psychiatry*. 11(1):91-100, 1976.

The influence of maprotiline or clomipramine on plasma tryptophan binding and brain tryptophan was studied in rats. Neither compound altered tryptophan binding nor brain tryptophan levels after acute or chronic treatment. In a comparative study maprotiline and clomipramine were administered to healthy volunteers for 4 days and the concentrations of total and free tryptophan in plasma were determined. Serotonin uptake was also measured in the platelets from these subjects. Maprotiline treatment did not inhibit serotonin uptake nor did it have any influence on plasma tryptophan binding. Clomipramine also had no influence on plasma tryptophan binding but strongly inhibited serotonin uptake into platelets. These results confirm the earlier observation that maprotiline has no influence on serotonin uptake and can be clearly distinguished from clomipramine. 17 references. (Author abstract)

001229 Gulati, O. D.; Shah, N. S.; Whitesides, D. B. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC Uptake of 3,4-dimethoxyphenylethylamine-1-14C (14C-DMPEA) by rat tissues in vitro. *Biological Psychiatry*. 11(1):75-84, 1976.

Rat heart and spleen slices were incubated with 3,4-dimethoxyphenylethylamine/1-14C (14C-DMPEA) in Krebs medium at 37C to determine whether DMPEA interacts with noradrenergic neuron. At the end of 5 to 20 min of incubation, the heart did not take up the radioactivity while the spleen did. The Km and Vmax values of uptake in the spleen were 1x10-4M and 20nmole/g per min, respectively, and the uptake was reduced to 16 to 35.1% in the cold (4C) and to 40.3 to 64% in Na+ free medium. Thus, the uptake was an energy dependent active process but was only partially Na+ dependent. Spleen slices incubated with 14C-dihydroxyphenylalanine free medium for 15 min following incubation with 14C-dihydroxyphenylalanine retained 41 to 74.8% of radioactivity. The uptake was insensitive to norepinephrine, dopamine, 5-hydroxytryptamine, cocaine, d-amphetamine, and normetanephrine. 6-Hydroxydopamine treatment of rats, which produced 93% reduction in the splenic norepinephrine content, did not significantly reduce uptake. Thus, the uptake of DMPEA into the spleen is not by adrenergic neurones. 19 references. (Author abstract modified)

001230 Haefely, W.; Ruch-Monachon, M.-A.; Jalfre, M.; Schaffner, R. Department of Experimental Medicine, F. Hoffmann-La Roche & Co., Ltd., Grenzacher Strasse 124, CH-4002 Basel, Switzerland Interaction of psychotropic agents with central neurotransmitters as revealed by their effects on PGO waves in the cat. *Arzneimittel-Forschung* (Aulendorf). 26(6):1036-1039, 1976.

The effects of various psychotropic drugs on ponto-geniculo-occipital (PGO) waves in the cat were studied. PGO waves were produced either by the i.p. administration of 20mg/kg of Ro 4-1284, a benzoquinolizine which impairs the storage of catecholamines and serotonin, or by two i.p. administrations of 300mg/kg p-chlorophenylalanine (PCPA), an inhibitor of serotonin synthesis. Tricyclic antidepressants depressed PGO waves by inhibiting neuronal uptake of serotonin. Some antipsychotic drugs increased PGO waves by blocking either serotonin or norepinephrine. Dextroamphetamine depressed PGO waves by releasing catecholamines, as did cocaine and mescaline. LSD, psilocybin, dimethyltryptamine, and bufotenin also depressed PGO waves, possibly by activating central serotonin receptors. Atropine depressed PGO waves, possibly by reducing the activity of norepinephrine neurons. Benzodiazepines increased PGO waves, probably by increasing the level of gamma-aminobutyric acid in the brain, which depressed the activity of norepinephrine. 12 references.

001231 Haigler, Henry James. Department of Pharmacology, Emory University, Atlanta, GA 30322 **Morphine: ability to block neuronal activity evoked by a nociceptive stimulus.** *Life Sciences (Oxford)*. 19(6):841-858, 1976.

The effect of morphine on the neuronal activity evoked by a nociceptive stimulus, a foot pinch, was studied in the dorsal raphe nucleus (DR) and in the mesencephalic reticular formation (MRF) of the rat. In the MRF and adjacent areas, neuronal firing was accelerated by the nociceptive stimulus. Morphine blocked this acceleration when administered either microiontophoretically or intravenously. Three lines of evidence indicate that this is a specific narcotic effect: naloxone, a specific narcotic antagonist, antagonized the effect of morphine; two morphine agonists, oxymorphone and methadone, blocked the evoked neuronal acceleration like morphine when administered either microiontophoretically or intravenously and naloxone also blocked the effects of the two agonists; and nonopioid central nervous system depressants did not block the acceleration in neuronal firing even though microiontophoretic ejection currents two to five times greater than those for morphine were used. In contrast, neuronal firing in the DR was rarely altered by the nociceptive stimulus or by morphine, administered either microiontophoretically or intravenously. Furthermore, morphine did not affect the inhibition produced by serotonin on neurons in the DR. It is concluded from this study that the MRF is a possible site of action for the antinociceptive effects of morphine. It is also concluded that morphine does not affect the spontaneous neuronal firing rate in the DR and that the DR is not a site of action of the antinociceptive effects of morphine when a foot pinch is used as the nociceptive stimulus. 43 references. (Author abstract modified)

001232 Hamburg, Martin D.; Kerr, Andrew. Department of Anatomy, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 **DDC-induced retrograde amnesia prevented by injections of dl-DOPS.** *Pharmacology Biochemistry and Behavior*. 5(4):499-501, 1976.

The mechanism by which the dopamine beta-hydroxylase inhibitor diethyldithiocarbamate (DDC) produces amnesia of trained passive avoidance responses was studied in rats. Injection of DDC 30 min prior to training of a passive avoidance task impaired performance of the task 24 hr later. Injection of DDC 30 min prior to testing also blocked retrieval of a passive avoidance habit trained in normal animals the previous day. Injection of the direct norepinephrine (NE) precursor dl-threo 3,4-dihydroxyphenylserine (DOPS) 60 min before DDC prevented both amnesias. The data support the hypothesis that reduced levels of NE are responsible for DDC induced amnesias. 28 references. (Author abstract modified)

001233 Hefti, F.; Lichtensteiger, W. Department of Pharmacology, University of Zurich, Zurich, Switzerland **An enzymatic-isotopic method for DOPA and its use for the measurement of dopamine synthesis in rat substantia nigra.** *Journal of Neurochemistry (Oxford)*. 27(2):647-649, 1976.

A method for enzymatic/isotopic assay was developed in analogy to the highly sensitive methods for the determination of catecholamines, concentrating on study of areas containing catecholamine cell bodies such as the dopamine neurons of substantia nigra. The assay method is designed to contribute to the elucidation of both the biochemical reactions of nerve cell bodies to neuronal activation and the interrelations between cell soma and dendrites which have also been found to contain dopamine. The principle of the assay method is methylation of DOPA by catechol-O-methyltransferase with S-adenosyl-Me-3-

methionine (SAM-3H) as donor, followed by separation of the 3-O-3H-methyl-DOPA from other catecholamine metabolites and unreacted SAM-3H on a cation exchanger. Use of the method after injection into substantia nigra of 3-hydroxybenzyl hydrazine showed DOPA accumulation linearly for 60 minutes, with its synthesis rate calculated and reflecting the combined synthesis rates of dopamine in dendrites and soma of zona compacta neurons and norepinephrine in terminals present in this area. Catecholamine concentrations were also assayed. A rate constant of synthesis can be calculated only on the basis of the total catecholamine concentration, reflecting mainly biosynthetic activity of dopaminergic neurons. It is concluded that the method developed is sensitive enough to study of accumulation of DOPA in small tissue samples from brain areas with relatively low catecholamine concentrations. 20 references.

001234 Hefti, F.; Lienhart, R.; Lichtensteiger, W. Dept. of Pharmacology, Univ. of Zurich, Gloriastr. 32A, CH-8006 Zurich, Switzerland **Transmitter metabolism in substantia nigra after inhibition of dopaminergic neurones by butyrolactone.** *Nature (London)*. 263(5575):341-343, 1976.

The similarities between terminal and somatodendritic areas that indicate a similar regulation of dopamine (DA) metabolism and an active role of DA in both parts of the neuron were studied in a situation where the dopaminergic neurones were inhibited. Gamma-butyrolactone (GBL) applied systemically strongly reduced unit activity of the dopaminergic neurones in zona compacta of rat substantia nigra. Results indicate that somatodendritic and terminal areas of dopaminergic neurones differ with regard to the regulation of monoamine metabolism at least in some functional states. It is suggested that the dopaminergic dendrites themselves probably respond to GBL in a way different from the reaction of terminals. 22 references.

001235 Henry, J. L.; Ben-Ari, Y. Department of Research in Anaesthesia, McGill University, 3655 Drummond Street, Montreal, Quebec, H3G 1Y6, Canada **Actions of the p-chlorophenyl derivative of GABA, Lioresal, on nociceptive and non-nociceptive units in the spinal cord of the cat.** *Brain Research (Amsterdam)*. 117(3):540-544, 1976.

The hypothesis that the para-chlorophenyl derivative of gamma-amino butyric acid (GABA) (baclofen, Lioresal) acts directly on the motoneurons as a specific antagonist to the excitatory actions of the proposed putative transmitter Substance P (sP) was investigated in cats. Microiontophoretically applied Lioresal had a reversible and reproducible depressant effect on the spontaneous discharge of all units tested. The drug also reduced the rate of discharge during the excitatory response induced by sP application and reduced the responses of nociceptive units to noxious cutaneous heat stimuli, an effect opposite to that of sP. However, while sP has an excitatory effect associated only with units responding to noxious stimuli, Lioresal caused a depression of all units tested. In addition, Lioresal depressed the excitatory responses of spinal units to the application of glutamate. It is suggested that Lioresal is not a specific antagonist to sP. 10 references.

001236 Hill, R. G.; Pepper, C. M. Department of Pharmacology, University of Bristol, Bristol BS8 1TD, England **The effects of morphine and met-enkephalin on nociceptive neurones in the rat thalamus.** *British Journal of Pharmacology (London)*. 58(3):459P-460P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of

morphine and metenkephalin on nociceptive neurons in the rat thalamus. Noxious stimuli used were immersion of tails in hot water or the pinch clamp method. Intravenous morphine prevented or greatly reduced the increased firing rate of nociceptive neurons produced by noxious stimulation. This was reversed by naloxone. Direct iontophoretic application of either morphine or metenkephalin to nociceptive neurons depressed spontaneous activity and prevented the excitation effects of noxious stimulation. The results seem to indicate that on this restricted population of neurons that the actions of morphine and metenkephalin are similar, and that enkephalin may function in brain as an endogenous morphine like factor. 9 references.

001237 Hillier, K.; Roberts, P. J.; Woollard, P. M. Department of Physiology and Biochemistry, University of Southampton, Southampton SO9 3TU, England Catecholamine-stimulated prostaglandin synthesis in rat brain synaptosomes. *British Journal of Pharmacology* (London). 58(3):426P-427P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed stimulation of prostaglandin synthesis in rat brain synaptosomes by noradrenaline, dopamine, and adrenaline. Noradrenaline, dopamine and adrenaline were found to substantially stimulate prostaglandin-E-2 synthesis in the rat brain while acetylcholine and 5-hydroxytryptamine were without stimulatory effect in this system. These results appear contradictory to previously reported work and suggests the link for prostaglandins exerting a positive feedback on noradrenaline release on central nerve terminals. 5 references.

001238 Hitzemann, Robert J.; Loh, Horace H. Langley Porter Neuropsychiatric Institute, Departments of Psychiatry and Pharmacology, University of California, San Francisco, CA 94134 On the possible role of brain protein synthesis in functional barbiturate tolerance. *European Journal of Pharmacology* (Amsterdam). 40(1):163-173, 1976.

The possible role of brain protein synthesis in functional barbiturate tolerance was studied. Pentobarbital pellet implantation increased more than 200% the ED50 dose of pentobarbital required to induce loss of the righting reflex within 2 min of i.p. injection and increased the onset of barbiturate induced sleep. Both tests of functional barbiturate tolerance were blocked by the intraventricular injection of cycloheximide. The effects of acute and chronic (pellet implantation) pentobarbital treatment on the incorporation of 3H-lysine (3Hlys) into the protein of various subcellular fractions of the cortex and sub-cortex were studied. In the subcortex, chronic pentobarbital treatment significantly stimulated protein synthesis 40%-50% in the microsomal, soluble and mitochondrial fractions. Both acute and chronic pentobarbital treatments significantly increased 3Hlys protein accumulation in a fraction of synaptic plasma membranes derived from a population of nerve ending particles enriched in gamma-aminobutyric acid. 36 references. (Author abstract modified)

001239 Hoffer, B. J.; Freedman, R.; Woodward, D. J.; Daly, J. W.; Skolnick, P. Laboratory of Neuropharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 Beta-adrenergic-control of cyclic AMP-generating systems in cerebellum: pharmacological heterogeneity confirmed by destruction of interneurons. *Experimental Neurology*. 51(3):653-667, 1976.

Rats subjected to neonatal x irradiation selectively lose the vast majority of late maturing granule, basket, and stellate cells, while the earlier maturing Purkinje cells remain intact.

These animals were used as a model to examine the electrophysiological and neurochemical interaction of neuroleptic compounds with the beta-adrenergically linked cyclic adenosine monophosphate (AMP) generating systems of cerebellum. Intracisternal injection of 6-hydroxydopamine in x irradiated animals resulted in an 80% increase in Purkinje cell mean discharge rate, suggesting an inhibitory adrenergic input comparable to that seen in normal animals. Iontophoresis of fluphenazine reversed the inhibitory effects of iontophoretically applied norepinephrine on Purkinje cell discharge rate in both x-irradiated animals and x-irradiated animals treated with 6-hydroxydopamine. The norepinephrine stimulated formation of cyclic AMP was significantly reduced in cerebellar slices prepared from x irradiated rats as compared with controls. Furthermore, while fluphenazine reduced the norepinephrine stimulated formation of cyclic AMP by 50% to 60% in cerebellar slices from control rats, the same concentration of fluphenazine reduced norepinephrine elicited accumulation of cyclic AMP to values which were not significantly different from basal values in slices from x irradiated rats. Results indicate that at least two populations of cells containing catecholamine sensitive cyclic AMP generating systems exist in the cerebellum. It is suggested that the locus of the neuroleptic inhibition of catecholamine sensitive cyclic AMP generating systems in the cerebellum appears to be postsynaptic, since the electrophysiological effects of fluphenazine were qualitatively similar in both x irradiated rats and x irradiated rats treated with 6-hydroxydopamine. 28 references. (Author abstract modified)

001240 Holtt, V.; Haarmann, I.; Herz, A. Abteilung für Neuropsychiatrie, Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany Identification of opiate/receptor binding in vivo. *Arzneimittel-Forschung* (Aulendorf). 26(6):1102-1104, 1976.

Binding to opiate receptors was studied in the intact mouse. Increasing amounts of an unlabeled antagonist with high affinity for the opiate receptor were injected i.v. with a constant, very small dose of the tritiated compound. The animals were sacrificed 15 min. after injection, their brains removed, and radioactivity determined by scintillation counter. At brain concentrations of 0.3nM, 75% of tritiated diprenorphine, 60% of tritiated naltrexone, and 50% of tritiated naloxone were displaced by high amounts of the unlabeled drugs. Similar results were obtained for receptor affinity in vitro. The number of binding sites in vivo was in the range of 10 pmoles/g brain. Tritiated agonists could be displaced only by unlabeled antagonists, not by unlabeled agonists. The maximum displacement is different in the various brain areas. The time course of the displacement differed for the various substances used. The displacement of tritiated etorphine by naltrexone could be correlated with the reversal of analgesia. 8 references.

001241 Honma, T.; Fukushima, H. Pharmaceuticals Division, Sumitomo Chemical Co., Ltd., 2-1, 4-Chome, Takatsukasa, Takarazuka, Hyogo 665, Japan Correlation between catalepsy and dopamine decrease in the rat striatum induced by neuroleptics. *Neuropharmacology* (Oxford). 15(10):601-607, 1976.

The correlation between drug induced catalepsy and striatal dopamine (DA) content was investigated in rats. The course of the development of catalepsy was well correlated with that of a decrease in DA in the corpus striatum after administration of haloperidol. The striatal DA was decreased by haloperidol in the same dose dependent manner as the catalepsy was intensified with increasing doses of the drug. By repeated administration of haloperidol or trifluoperidol the catalepsy was inten-

sified, and the DA decrease in the rat striatum was extended. With repeated administration of ID-4708, a new butyrophenone compound, the intensity of catalepsy and the DA decrease induced by its initial administration was little altered. Oral administration of chlorpromazine produced moderate catalepsy and decreased striatal DA. No catalepsy or only slight catalepsy was observed after the administration of thioridazine, clozapine and sulpiride, and a decrease of DA in the striatum did not occur. 30 references. (Author abstract modified)

001242 Horng, Jong S.; Smits, Stephen E.; Wong, David T. Lilly Research Labs, Eli Lilly and Company, Indianapolis, IN 46206 The binding of the optical isomers of methadone, alpha-methadol, alpha-acetylmethadol and their N-demethylated derivatives to the opiate receptors of rat brain. *Research Communications in Chemical Pathology and Pharmacology*. 14(4):621-629, 1976.

The optical isomers of methadone, alpha-methadol, alpha-acetylmethadol and their N-demethylated derivatives were systematically studied for their effects on the binding of 3H-dihydromorphine (3H-DHM) and 3H-naloxone (3H-NLX) to opiate receptors in rat brain homogenate. The relative affinities of these agents in competing for both 3H-DHM and 3H-NLX binding parallel their analgesic effects. l-Methadone is about 30 times as effective as d-methadone in competing for both 3H-DHM and 3H-NLX binding sites. The reduction of l-methadone to alpha-d-methadol and subsequent N-demethylation to alpha-d-normethadol reduce its effectiveness as indicated by the increase in the IC50 values for both 3H-DHM and 3H-NLX binding. The reduction of d-methadone followed by N-demethylation produces a potent derivative, alpha-l-normethadol, which has IC50 values on 3H-DHM and 3H-NLX binding similar to those of l-methadone. The affinity of alpha-l-acetylmethadol on the binding of both 3H-ligands falls between those of l-methadone and d-methadone, and increases as it is N-demethylated. Alpha-d-acetylmethadol is more effective than alpha-l-acetylmethadol in competing for both 3H-ligands from the opiate receptors, and its affinity, unlike that of alpha-l-acetylmethadol, decreases when it is N-demethylated. The affinities of the methadone isomers and related compounds on the binding of 3H-NLX fall in the presence of sodium plus. The latter property indicates the agonistic nature of this series of drugs. 20 references. (Author abstract)

001243 Hui, Koon-Sea. Dept. of Pharmacology, Faculty of Medicine, University of Hong Kong, 5 Sassoon Rd., Hong Kong The effect of thiazol-4-ylmethoxyamine, a histidine decarboxylase inhibitor, on the development of morphine tolerance and physical dependence in mice. *Experientia (Basel)*. 32(10):1313-1315, 1976.

The effect of thiazol-4-ylmethoxyamine (TMA), a potent histidine decarboxylase inhibitor, on the development of morphine tolerance and physical dependence in mice was investigated. Mice were made dependent on morphine by implantation of morphine pellets. Tolerance was measured by the tail flick test, and physical dependence was assessed by naloxone challenge. TMA was administered in doses of 100mg/kg i.p. 48 hours before morphine pellet implantation. Results indicate that TMA inhibited the development of morphine tolerance and physical dependence. This action is likened to that of cycloheximide, and it is noted that TMA is as potent as cycloheximide in preventing tolerance, but is only 20% as effective in inhibiting physical dependency. It is suggested that morphine tolerance and physical dependence both have underlying mechanisms which depend on the formation of histamine somewhere in the brain.

001244 Huidobro, F.; Huidobro-Toro, J. P.; Way, E. Leong. Department of Pharmacology, Institute of Biological Sciences, Catholic University of Chile, Santiago, Chile Studies on tolerance developed to single doses of morphine in mice. *Journal of Pharmacology and Experimental Therapeutics*. 198(2):318-329, 1976.

Single dose tolerance of mice to the antinociceptive effect of morphine can be demonstrated using an adequate initial priming dose of morphine and allowing an interval of 48 to 72 hours for its development. The threshold dose necessary to produce tolerance was found to be about 3 to 4 times greater than that for producing analgesia but higher doses of morphine did not enhance further tolerance development. Evidence of tolerance was indicated by the fact that when the antinociceptive response to morphine was assessed by the hotplate and the tail flick procedures, a shift in the dose response curve of morphine to the right occurred after an adequate single priming dose of morphine. Cross-tolerance was evidenced by a decrease in analgesic response to methadone 3 days after a single priming dose of morphine and a decrease in morphine response after a single dose of methadone. The development of a single dose tolerance was inhibited by cycloheximide. Single dose tolerance was also blocked by 5, 6-dihydroxytryptamine and perhaps enhanced by L-tryptophan. Cyclic 3',5'-adenosine monophosphate did not affect single dose tolerance development significantly although the direction was in favor of augmentation. Morphine uptake by the brain was not modified by the development of single dose tolerance. Physical dependence, as measured by naloxone precipitated withdrawal jumping, was not observed when single dose analgesic tolerance was maximal. The results suggest that single dose tolerance to morphine involves the synthesis of some macromolecule and support previous findings in the laboratory involving an association with serotonin. 49 references. (Author abstract)

001245 Humphreys, R. B.; Hawkins, M.; Lipton, J. M. Department of Psychiatry, University of Texas Health Science Center, Dallas, TX 75235 Effects of anesthetic injected into brainstem sites on body temperature and behavioral thermoregulation. *Physiology and Behavior*. 17(4):667-674, 1976.

In order to assess whether differential effects upon physiological and behavioral thermoregulation are produced by temporarily depressing brain activity with an anesthetic, five brain regions were examined in 45 male albino rats. These included: the preoptic/anterior hypothalamic region (PO/AH), the posterior (PH) and lateral hypothalamic (LH) regions, the mesencephalic reticular formation (MRF) and the medulla oblongata (MED). The rectal temperature (Tre) of rats with central cannulae was recorded after sodium pentobarbital injections while the animals rested in 23 degree, 10 degree, and 34 degree C environments. In other experiments the effects of central anesthetic injections on behavioral regulation against heat were measured. Anesthetic injected into the PO/AH region caused changes in Tre and behavior that are consistent with a coordinated rise in the set point of body temperature control. Injections into the MED produced transient and rapid decreases in Tre without affecting behavioral thermoregulation. Bilateral injections into the LH caused hyperthermia in the 10 degree and 34 degree C environments, hypothermia in the 23 degree C environment, and had no effect on behavioral temperature regulation. No changes in thermoregulatory responses were observed after PH and MRF injections. These results indicate that there are differences among the five brain regions in relative importance to overall temperature control and specific differences in the significance of certain regions

to the two forms of temperature control, physiological and behavioral temperature regulation. 31 references. (Author abstract modified)

001246 Hyttel, J.; Nielsen, I. Møller. Research Laboratories, H. Lundbeck & Co. A/S, Østtilvej 7-9, DK-2500 Copenhagen-Valby, Denmark **Changes in catecholamine concentrations and synthesis rate in mouse brain during the 'supersensitivity' phase after treatment with neuroleptic drugs.** *Journal of Neurochemistry* (Oxford). 27(1):313-315, 1976.

The ability of neuroleptics to increase ¹⁴C-catecholamine accumulation in the mouse brain in the supersensitivity phase after a single dose of teflutixol or after repeated haloperidol treatment is studied. Results indicating that the response to neuroleptic treatment is the same in untreated and pretreated animals suggests that the decreased sensitivity to the neuroleptic cannot explain the development of tolerance after treatment with neuroleptics. It is suggested that an increased sensitivity to dopamine (DA) and DA agonist could account for three of the results observed. 13 references.

001247 Ingoglia, N. A.; Sellin, L. C.; Lindquist, T. D. Departments of Physiology and Neuroscience, New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 **The effect of cordycepin on the appearance of (3H)RNA in the goldfish optic tectum following intracocular injection of (3H)uridine.** *Journal of Neurochemistry* (Oxford). 27(1):179-184, 1976.

Cordycepin was injected into the right eye of goldfish prior to the injection of radioactive RNA precursors into the same eye and the effect of this drug on the appearance of radioactive nucleotides and RNA in the contralateral optic tectum was determined. Results showed that cordycepin significantly decreased the amount of RNA appearing in the contralateral optic tectum while decreasing the levels of transported TCA soluble material to a lesser degree. These results are discussed as evidence supporting the concept of axonal transport of RNA in normal goldfish optic nerves. 32 references.

001248 Ishida, Yukio; Watanabe, Kouzo; Kobayashi, Shigeru; Kihar, Masaru. Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, University of Tokushima, Tokushima, Tokushima 770, Japan **Selective alpha-adrenoceptor blocking actions of a new derivative of 2-halogenoethylamine: 6-(2-bromoethyl)-10,11-methylenedioxy-5,6,7,8-tetrahydrodibenz(c,e)azocine.** *Japanese Journal of Pharmacology* (Kyoto). 26(5):607-614, 1976.

A new compound, 6-(2-bromoethyl)10,11-methylenedioxy-5,6,7,8-tetrahydrodibenz(c,e)azocine (DA-VIII-MBr) was found to have a more selective alpha-adrenergic blocking action than dibenamine or phenoxybenzamine. From dose/response curves for adrenaline and 5-hydroxytryptamine (5-HT) obtained in strips of rat aorta before and after incubation with each of the three blocking agents, the fractions of receptors remaining active for adrenaline and 5-HT, respectively, were estimated. After blockade with DA-VIII-MBr the receptors for adrenaline were blocked considerably, but those for 5-HT were little affected. Dibenamine blocked the receptors for adrenaline and 5-HT almost equally. The effective dose of phenoxybenzamine for adrenaline receptors was less than one hundredth that of dibenamine or DA-VIII-MBr, but specificity for these receptors was intermediate between those of dibenamine and DA-VIII-MBr. The structure of DA-VIII-MBr is an analog of apogalanthamine and its nitrogen atom bears the 2-halogenoethylamine group in part of an eight membered ring. 30 references. (Author abstract)

001249 Ishitani, R.; Iwamoto, T. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Josai Univ., 1076 Tawame, Sakado, Saitama 350-02, Japan **Distribution of H3-dimetacrine in rat cerebral cortex by electron microscopic autoradiography.** *Experientia* (Basel). 32(10):1306-1308, 1976.

The cellular distribution of H3-dimetacrine in rat cerebral cortex was investigated by electron microscopic autoradiography. Male Wistar rats were administered H3-dimetacrine by direct lateral intraventricular injection and were sacrificed for brain examination 1 hour posttreatment. Results show that the drug was located primarily in the synaptic regions, although dendrites, axons, glial, and neuronal cells absorbed some, also. It is suggested that dimetacrine may be associated with nerve ending function and that such interactions may affect synaptic transmission, thus producing the observed behavioral effects of this tricyclic antidepressant.

001250 Ito, Tsugutaka; Shimizu, Masanao. Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Suita, Osaka 564, Japan **Effect of psychotropic drugs on caudate spindle in cats.** *Japanese Journal of Pharmacology* (Kyoto). 26(5):527-534, 1976.

To ascertain whether neuroleptics act on the caudate nucleus itself, the effects of neuroleptics as well as other centrally acting drugs were examined in relation to caudate spindle and electroencephalographic arousal responses (sciatic nerve stimulation) in gallamine immobilized cats. Haloperidol and chlorpromazine enhanced the caudate spindle at a dose which had no effect on the EEG arousal response. On the other hand, clozapine and a higher dose of chlorpromazine enhanced the caudate spindle, but depressed the arousal response. High frequency stimulation of the sciatic nerve suppressed the caudate spindle. Pentobarbital, biperiden and diazepam, while depressing the arousal response, caused an enhancement of the caudate spindle. Imipramine at a low dose had no effect on either response, whereas at a high dose this drug enhanced the caudate spindle with concomitant depression of the arousal response. From these results, it is concluded that the enhancing action on the caudate spindle induced by haloperidol and a low dose of chlorpromazine is due to an increase in susceptibility of the caudate nucleus itself. In addition, it is suggested that depression of the activating system is involved in an appearance of the caudate spindle. 22 references. (Author abstract)

001251 Itoh, Masatoshi; Uchimura, Hideyuki; Hirano, Makoto; Saito, Masashi; Nakahara, Tatsuo. Department of Neuropsychiatry, Kyushu University, Fukuoka, 812, Japan **Effects of reserpine and pargyline on glutamate decarboxylase activity in rat hypothalamic nuclei.** *Brain Research* (Amsterdam). 115(3):529-534, 1976.

The changes of glutamate decarboxylase (GAD), a gamma-aminobutyric (GABA) synthesizing enzyme, activity in the hypothalamic nuclei of reserpine treated or pargyline treated rats were examined in an investigation of the functions of GABA and the interaction between GABA and monoamines in the hypothalamic nuclei. In the nucleus ventromedialis, pargyline treatment resulted in a significant decrease of GAD activity and also reserpine produced a decrease of GAD activity but it was not significant. In contrast, the GAD activity in the medial part of the lateral hypothalamic area increased significantly by reserpine pargyline treatment. On the other hand, aphagia and marked weightloss were observed similarly after the chronic administrations of both drugs. The finding, that a marked elevation of GAD activity in the nucleus arcuatus is induced by reserpine, provides the possibility that the interac-

tion between GABA and biogenic amines may exist in the nucleus arcuatus and GABA is likely to act as a modulator of the secretions of some hormone releasing factors. On the other hand, GAD activity in the nucleus arcuatus did not change by pargyline treatment. However, pargyline may block the elevation of GAD activity in this nucleus of reserpine treated rats, because the activation of CRF secretion and the inhibition of ovulation induced by reserpine are blocked by pargyline. GAD activity in the nucleus posterior was elevated significantly by the chronic pargyline treatment. Thus, the findings suggest that GABA, in a certain hypothalamic nucleus, is likely to have a specific function, and also the interaction between GABA and monoamines may exist in the nuclei of arcuatus and posterior. Further studies, however, are necessary to explain the regulatory mechanisms of the hypothalamic functions by GABA containing neurons. 29 references.

001252 Jacob, J. J.; Michaud, G. M. Service de Pharmacologie et Toxicologie, Institut Pasteur 28, rue de Dr. Roux, F-75015 Paris, France /Morphine-opposed effects of naloxone in unanesthetized dogs./ Production par la naloxone d'effets inverses de ceux de la morphine chez le chien éveillé. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 222(2):332-340, 1976.

In unanesthetized dogs naloxone induced effects opposed to those of morphine (tachycardia, agitation, hyperthermia, tachypnea) and mydriasis were studied. These effects were moderate transient; after repeated administrations, acute tolerance developed, and some moderate morphine like effects (miosis, sedation) were observed. The stimulatory effects described here may result from an antagonism of a morphinomimetic natural ligand and represent thus indirect arguments in favor of normal functions of this ligand; these functions would be to temper not only algesic but also other stimulant reactions. The limitation of the effects might result from the limited release of this ligand in normal dogs and/or from interfering morphinomimetic properties of naloxone, which are apparently unmasked when administrations are repeated. Both, stimulatory and inhibitory effects of naloxone are not liable to represent noticeable side-effects of this drug, but they both might play some role in the mechanisms of precipitated abstinence. 22 references. (Author abstract)

001253 Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 Minireview: an animal behavior model for studying central serotonergic synapses. Life Sciences (Oxford). 19(6):777-786, 1976.

An animal behavior model for studying the functional activity in central serotonin mediated synapses is described. It is produced by compounds which either increase synaptic serotonin content or stimulate serotonin receptors, and consists most conspicuously of tremor, rigidity, reciprocal forepaw treading, Straub tail, hindlimb abduction, and lateral head weaving. Evidence is available to indicate that it has specificity in reflecting only the activity in the serotonin system. The neuronal substrates that mediate the elaboration of the component signs are localized exclusively in the lower brainstem and spinal cord. Although it has been studied most extensively in the rat, a similar response pattern is also seen in a number of different species. It has been implemented as a useful tool in studying phenomena as diverse as: the effect of hypothalamic factors on neurotransmission; the metabolism of serotonin; the action of therapeutic and psychoactive drugs; the pharmacology of central serotonin receptors; the actions of lysergic acid diethylamine; and the development of denervation supersensitivity in the central serotonin system. 40 references. (Author abstract modified)

001254 Jeffrey, P. L.; Gibbs, M. E. Department of Biochemistry, Monash University, Clayton Victoria, 3168 Australia Biochemical actions of sympathomimetic drugs which overcome cycloheximide-induced amnesia. Pharmacology Biochemistry and Behavior. 5(5):571-575, 1976.

The effects on Na/K ATPase activity in total homogenate of chicken forebrain of several sympathomimetic drugs which had previously been found to overcome the amnesic action of cycloheximide (CXM) were investigated in vitro. Norepinephrine (NE) and the beta-adrenergic receptor stimulant isoproterenol significantly stimulated the activity of the enzyme, while the beta-adrenergic receptor blocker propranolol inhibited activity. Amphetamine, the alpha-adrenergic receptor stimulant methoxamine, and the alpha-adrenergic receptor blocker piperoxane had no effect on enzyme activity. In a purified synaptosomal preparation, both amphetamine and NE produced a slight stimulation of enzyme activity. Amphetamine did not inhibit radiolabeled leucine uptake or incorporation into protein in the synaptosomal fraction, nor was it able to alleviate CXM inhibition of radiolabeled leucine incorporation into synaptosomal protein. It is suggested that amphetamine (via release of NE), NE and isoproterenol act by stimulating and maintaining the labile, sodium pump dependent, phase of memory formation for a sufficient length of time until protein synthesis inhibition by CXM wears off. 20 references. (Author abstract modified)

001255 Johnson, Kenneth M.; Dewey, William L.; Ho, Beng T. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 In vitro alteration of the subcellular distribution of 3H-reserpine in the rat forebrain by delta9-tetrahydrocannabinol. Research Communications in Chemical Pathology and Pharmacology. 15(4):655-671, 1976.

Delta9-tetrahydrocannabinol (delta9-THC) inhibition of the action of reserpine by altering its normal distribution in various membrane components of the brain was investigated in the rat brain in vitro. Preincubation with delta9-THC produced a shift in the localization of 3H-reserpine from the incubation medium and the microsomal supernatant to the crude mitochondrial (CM) pellet. Although the concentrations of reserpine increased in the three CM fractions containing myelin, membrane fragments or mitochondria, much larger increases occurred in the two fractions containing cholinergic nerve endings and noncholinergic nerve endings. Morphine, serotonin, sodium pentobarbital, cocaine, amphetamine, imipramine, chlorpromazine, tetrabenazine and reserpine, all of which are believed to have membrane mediated mechanisms, had no effect on the amount of reserpine bound to the crude mitochondrial fraction. It is concluded that delta9-THC may retard some of the effects of reserpine by increasing or stabilizing the amount of reserpine bound nonspecifically to the neuronal membranes, thereby shifting the proposed equilibrium between the specific and nonspecific sites towards the latter. 17 references. (Author abstract modified)

001256 Joseph, M. H.; Emson, P. C. Division of Psychiatry, MRC Clinical Research Centre, Watford Rd., Harrow, Middlesex HA1 3UJ, England Taurine and cobalt induced epilepsy in the rat: a biochemical and electrocorticographic study. Journal of Neurochemistry (Oxford). 27(6):1495-1501, 1976.

The effects of peripheral and central, chronic and acute, taurine administration on the number of epileptic spikes in cobalt induced epilepsy were investigated in rats. The effects of cobalt implantation and oral taurine on levels of brain amino acids were also studied. Results show that taurine levels

around epileptic foci induced by cobalt implantation was reduced 8 to 10 days postoperation, the time of maximal spike activity in the electrocorticogram. Levels returned to normal at later times. This pattern was seen not only in the primary focus, but also to a lesser extent in the secondary focus in the contralateral cortex. Acute administration of taurine intraperitoneally or intraventricularly resulted in at most transient effects on epileptic spiking. Chronic oral taurine elevated brain taurine in normal rats only after prolonged administration, but in cobalt treated rats it prevented the fall of taurine in the secondary focus, and reduced the extent and duration of the fall in the primary focus. Nonetheless, chronic oral or intraventricular administration failed to modify the development of spike activity. At 11 days after implantation, chronic oral taurine did not significantly reverse the falls in transmitter amino acids in the primary focus. It is concluded that taurine is ineffective in altering the development or expression of this type of cobalt induced epilepsy in the rat, in spite of adequate penetration to the brain. Possible reasons for these findings are discussed. 35 references. (Author abstract modified)

001257 Kaariainen, Ilpo; Vikberg, Pasi. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Effects of aminooxyacetic acid and baclofen on catalepsy, striatal homovanillic acid increase and antinociception caused by methadone in rats.** *Acta Pharmacologica et Toxicologica* (Kobenhavn). 39(5):536-544, 1976.

The effects of aminooxyacetic acid (AOAA), which increases the cerebral concentration of gamma-amino-butyric acid (GABA), and baclofen, a structural analogue of GABA, on the catalepsy, striatal homovanillic acid (HVA) increase, and antinociception caused by methadone were studied in rats. Antinociceptive responses were tested by the electric foot shock method. A new stimulator unit, which delivers nearly constant current over a wide range of output voltage and is noiseless was designed, and its construction is described. AOAA and baclofen did not alter the methadone induced catalepsy. AOAA alone did not alter striatal HVA content and had no effect on the methadone induced HVA increase. Baclofen increased striatal HVA by 19% but reduced the methadone induced HVA increase by 36%. AOAA and baclofen had no antinociceptive effect but significantly increased the antinociception caused by methadone. It is suggested that narcotic analgesics might cause catalepsy and increase striatal dopamine turnover by a different mechanism than do neuroleptic drugs. The results support the hypothesis that GABA may be involved in pain mechanisms. 24 references. (Author abstract modified)

001258 Kappus, H. Institut für Toxikologie der Universität Tübingen, Wilhelmstr. 56, D-7400 Tübingen, Germany **Irreversible protein binding of 14-C-imipramine in rats in vivo.** *Archives of Toxicology* (Berlin). 37(1):75-80, 1976.

Irreversible protein binding of imipramine, previously found to occur in vitro, was studied in vivo in rats. After a single dose of radiolabeled imipramine, radioactivity could be measured in the following organs in decreasing order of activity: liver, kidney, serum, fat, spleen, duodenum, lung, muscle and brain. Liver microsomes contained the largest portion of radioactivity derived from the drug. After exhaustive extraction, only proteins in liver, kidney, spleen, lung and serum contained measurable amounts of radioactive labeling. The greatest amount of imipramine irreversibly bound to proteins was detected in liver microsomes. The possibility that irreversible protein binding of imipramine may result in toxic side effects is discussed. 21 references. (Author abstract modified)

001259 Karobath, M. Psychiatrische Universitätsklinik, Lazarettgasse 14, A-1097 Wien, Austria **The dopamine receptor and antipsychotic effect./ Dopaminrezeptor und antipsychotische Wirkung.** *Arzneimittel-Forschung* (Aulendorf). 26(6):1029-1030, 1976.

A report on a workshop on dopamine receptors and the antipsychotic effect of major tranquilizers is given. The effect of various antipsychotic drugs on the dopamine mediated adenylyl-cyclase system is considered. A perfect correlation was obtained between the antipsychotic activity of drugs in vivo and the inhibition of dopamine release. A dose of 50mg/kg clozapine does not induce tolerance, but a dose of 100mg/kg clozapine does induce tolerance; this is due to increased dopamine turnover. Clozapine has anticholinergic effects in the brain. It is speculated that the simultaneous use of a neuroleptic drug and an anticholinergic may produce tardive dyskinesia.

001260 Karpiak, Stephen E.; Graf, Liselotte; Rapport, Maurice M. Division of Neuroscience, New York State Psychiatric Institute, NY **Antiserum to brain gangliosides produced recurrent epileptiform activity.** *Science*. 194(4266):735-736, 1976.

The effect of antiserum to brain gangliosides on the brains of rats was measured electroencephalographically. A single injection of the antiserum onto (and into) the sensorimotor cortex of the rat resulted in recurrent spiking in the cortical electroencephalogram lasting from 7 to 17 days. Absorption of antibody with pure monosialoganglioside completely abolished the effect. Spiking was reactivated after 4 weeks by intramuscular injection of pentylenetetrazole. It is suggested that this immunological technique may be useful as a model for studying epilepsy. 15 references. (Author abstract modified)

001261 Kehr, W. Department für Neuropsychopharmakologie, Schering AG, Müllerstrasse 170-178, D-1000 Berlin 65, Germany **Reciprocal action of dopamine receptor agonists and antagonists with regard to dopamine synthesis and metabolism./ Wechselwirkung von Dopaminrezeptoragonisten und -antagonisten hinsichtlich Dopaminsynthese und -metabolismus.** *Arzneimittel-Forschung* (Aulendorf). 26(6):1086-1088, 1976.

The interaction of agonists and antagonists at the dopamine receptor was studied. In doses of 0.3 to 10mg/kg i.p., d-amphetamine stimulated the formation of dopa in the dopamine rich areas of the corpus striatum and mesolimbic cortex in the rat. In the neocortex, 0.3 to 3mg/kg d-amphetamine had no effect on dopamine formation, but 10mg/kg caused a decrease in dopamine formation. Combination of the agonist d-amphetamine with the antagonist haloperidol caused increased dopamine synthesis in the rat forebrain after inhibition of amino acid decarboxylase with 3-hydroxybenzylhydrazine (NSD 1015). Amphetamine (10mg/kg) and haloperidol (0.5mg/kg) both caused a threefold increase in methoxytyramine formation after pretreatment with 100mg/kg pargyline i.p. Amphetamine, 1mg/kg, potentiated the haloperidol induced formation of 3-methoxytyramine, and 10mg/kg led to further potentiation. Thus, haloperidol and amphetamine have synergistic action on dopamine synthesis and dopamine release. 7 references.

001262 Kim, Haing-Ja; Routtenberg, Aryeh. Cresap Neuroscience Laboratory, Northwestern University, Evanston, IL 60201 **Retention disruption following post-trial picrotoxin injection into the substantia nigra.** *Brain Research* (Amsterdam). 113(3):620-625, 1976.

The mechanism by which treatments that alter the physiological activity of the mammalian brain can disrupt memory when administered shortly after learning were investigated in rats. Injections of picrotoxin into the substantia nigra 5 minutes after learning of passive avoidance behavior, but not 22 hours later, disrupted retention of the learned task. Doses of picrotoxin too small to produce convulsions or induce circling behavior were effective in producing the amnesic effect. Strychnine injected into the same location had no effect on retention. It is suggested that: 1) the amnesic effect of picrotoxin is not likely to be associated with the ability of the drug to cause convulsion or circling behavior; 2) the retention deficit due to picrotoxin is due to an effect on memory consolidation processes rather than retrieval processes; and 3) the retention deficit produced by picrotoxin is probably due to an interaction of the drug with the gamma-aminobutyric acid mediated inputs to the substantia nigra, rather than to a non-specific CNS stimulant effect. 39 references.

001263 Klee, Werner A. Laboratory of General and Comparative Biochemistry, Building 36, National Institute of Mental Health, Bethesda, MD 20014 Opiates and cyclic AMP. (Unpublished paper) Washington, DC, NIMH, 1976. 17 p.

The research providing evidence that opiates may function via the adenylate cyclase system is summarized and discussed. The evidence indicates that narcotics have two effects upon adenylate cyclase; i.e. an immediate inhibition followed by a slowly developing increase in total activity. It is suggested that this dual regulation can account for all of the known effects of these drugs, although other contributory mechanisms cannot be ruled out at present. 56 references.

001264 Klemm, W. R.; Mallari, C. G.; Dreyfus, L. R.; Fiske, J. C.; Forney, E.; Mikeska, J. A. Dept. of Biology, Texas A & M University, College Station, TX 77843 Ethanol-induced regional and dose-response differences in multiple-unit activity in rabbits. *Psychopharmacology* (Berlin). 49(3):235-244, 1976.

The effects of ethanol on spontaneous multiple unit activity (MUA) from various rabbit brain sites that were monitored simultaneously were evaluated to determine if neurons in various brain areas are differentially sensitive to ethanol and to identify the general location of such target sites. Each of the 12 rabbits received intraperitoneal injections of 300mg/kg, 600mg/kg, 900mg/kg, and 1200mg/kg of 20% ethanol and a saline control injection given in random order with at least a 4 day interval between injections. Large amounts of MUA data, recorded continuously for a preinjection control period and a postinjection period, were quantified by a sensitive and unique technique. MUA changes did not correlate with alcohol induced changes in the corresponding electroencephalograph (EEG) for the same locus. Whereas visual inspection of the EEG did not disclose any regional differences in response to ethanol, both temporal and topographical differences in ethanol effect on MUA were observed. There were histologically verified brain areas with adequate sample size for statistical evaluation of MUA response. At high doses, all brain areas were affected. Included among the brain areas which were least affected by low doses were the caudate nucleus, septum, fornix, and medial forebrain bundle. Those areas that met the criteria for target sites of responding quickly to low doses were: cerebellar cortex, cerebral cortex, hippocampus, lateral and medial geniculate nuclei, midbrain reticular formation, and pyriform cortex. In conjunction with a preliminary study, the data indicate that the most ethanol sensitive tissue is found in the various kinds of cortex, cerebellar and cerebral (both paleocortex and neocortex). 31 references. (Author abstract modified)

001265 Koe, B. Kenneth. Department of Pharmacology, Pfizer, Inc., Groton, CT 06340 Molecular geometry of inhibitors of the uptake of catecholamines and serotonin in synaptosomal preparations of rat brain. *Journal of Pharmacology and Experimental Therapeutics*. 199(3):649-661, 1976.

The effects of several compounds with relatively rigid molecular structure on uptake of dopamine (DA) and serotonin (5-HT) by synaptosomal preparations of rat corpus striatum and on uptake of norepinephrine (NE) by synaptosomal preparations of rat hypothalamus was investigated. Comparison of the relative monoamine uptake blocking effects of 1R, 4S-N-methyl-4-phenyl-1, 2,3,4-terahydro-1-naphthylamine (CP-24,441), 4-phenylbicyclo2.2.2octan-1-amine (EXP-561), nomifensine and nefopam suggests some structural and steric requirements for monoamine uptake inhibitors, which are described and discussed. It is suggested that the actual potency of a given compound is modulated by additional structural and stereochemical factors. 54 references.

001266 Koller, W. C.; Berry, C. A. Dept. of Pharmacology, Northwestern University Medical School, Chicago, IL 60611 Alteration of basal ganglia evoked responses by reserpine and L-dopa. *Psychopharmacology* (Berlin). 49(3):281-285, 1976.

Macroelectrode techniques were used to define basal ganglia sensitivity to drugs which alter dopamine levels, and evoked responses were recorded between basal ganglia structures before and after systemic administration of reserpine and L-dopa in cats. The caudate response resulting from substantia nigra stimulation and the substantia nigra response elicited by globus pallidus stimulation were increased at several hours after the systemic administration of reserpine. L-dopa in the presence of dopa decarboxylase inhibition (MK-486) depressed these responses and reversed the effect of reserpine at 0.5 hours after administration. Reserpine did not reverse the L-dopa effect. Reserpine and L-dopa caused no significant change in responses between other basal ganglia structures. These data give evidence that the basal ganglia are major sites for reserpine and L-dopa action. 35 references. (Author abstract modified)

001267 Kruk, Z. L.; Zarrindast, M. R. Department of Pharmacology and Therapeutics, London Hospital Medical College, Turner Street, London E1 2AD, England Mazindol anorexia is mediated by activation of dopaminergic mechanisms. *British Journal of Pharmacology* (London). 58(3):367-372, 1976.

The activation of dopaminergic mechanisms as a mediator of mazindol anorexia was studied in rats. Anorexia produced by injections of mazindol could be antagonized by pretreatment with a dopamine receptor blocker, but not by pretreatment with an alpha-adrenoceptor blocker, a beta-adrenoceptor blocker, or a 5-hydroxytryptamine receptor blocker. In rats with a unilateral lesion in the substantia nigra, mazindol caused a dose dependent turning toward the lesioned side which could be antagonized by pretreatment with a dopamine receptor blocker. Pretreatment with reserpine and alpha-methyl-p-tyrosine prevented any motor stimulant action by mazindol. In vitro studies indicated that mazindol blocks uptake and cause release of dopamine. The results suggest that the anorectic action of mazindol is mediated by a dopaminergic mechanism. 18 references. (Author abstract modified)

001268 Kuromi, Hiroshi; Satoh, Masamichi; Takagi, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan Inhibition of thalamic and hypothalamic somatosensory evoked potentials by stimulation of substantia nigra and its modification by morphine

and methotrimeprazine (levomepromazine). Japanese Journal of Pharmacology (Kyoto). 26(3):331-337, 1976.

A brief electrical stimulation of the substantia nigra induced a marked and long-lasting inhibition of the somatosensory evoked potentials recorded from the centrum medianum of the thalamus (CM) and posterior hypothalamic area (PHA) following sciatic stimulation in unanesthetized rabbits. The nigral inhibitory effect on CM was prolonged by the administration of morphine, but not influenced by that of methotrimeprazine. The nigral inhibitory effect on PHA was enhanced by the injection of methotrimeprazine, but not changed by that of morphine. The results indicate that the inhibitory system originating from the substantia nigra operates on the somatosensory transmissions from the peripheral nerve to the thalamus and hypothalamus, and that morphine or methotrimeprazine in small doses induces a selective potentiation of the nigral inhibitory influence on the thalamus or hypothalamus, respectively. 8 references. (Author abstract modified)

001269 Ladinsky, H.; Consolo, S.; Bianchi, S.; Jori, A. Istituto di Ricerche Farmacologiche Mario Negri, Via Eritrea 62, I-20157 Milan, Italy Increase in striatal acetylcholine by picrotoxin in the rat: evidence for a gabergic-dopaminergic-cholinergic link. Brain Research (Amsterdam). 108(2):351-361, 1976.

The hypothesis that the disinhibition of dopaminergic neurons through a blockade of GABA receptors by picrotoxin could lead to an inhibition of cholinergic neurons and an increase in acetylcholine content was investigated. Picrotoxin, a GABA receptor blocking agent, increased rat striatal acetylcholine content without altering the levels of this amine in the cerebral hemispheres, mesencephalon, diencephalon, hippocampus and cerebellum. Striatal choline levels were concomitantly decreased. Picrotoxin also increased striatal homovanillic acid levels, an effect which was not antagonized by pretreatment with the dopamine receptor stimulating agent, piribedil. Picrotoxin did not affect striatal choline-O-acetyltransferase activity or cholinesterase activity after *in vitro* incubation. The action of picrotoxin on striatal acetylcholine levels was partially antagonized by pimozone and completely blocked by alpha-methyl-para-tyrosine pretreatment while the intraventricular injection of 6-hydroxydopamine was without effect. Convulsions were not prevented by any of these treatments. It is suggested that picrotoxin releases dopamine through disinhibition of the dopaminergic neurons as a result of blockade of gabergic receptors. The increased dopaminergic activity inhibits cholinergic neurons and leads to an increase in acetylcholine content. The data thus provide evidence for a possible gabergic (inhibitory)/dopaminergic (inhibitory)/cholinergic link terminating in the striatum. 52 references. (Author abstract modified)

001270 Lamboeuf, Y.; de Saint-Blanquat, G.; Derache, R. Groupe de Recherches sur la Toxicologie des Aliments et des Boissons INSERM, 2, rue François Magendie, F-31400 Toulouse, France Secretion and irrigation of gastric mucosa during disulfiram effect: experimental study in the dog. Arzneimittelforschung (Aulendorf). 26(7):1344-1347, 1976.

The effect of ethyl alcohol and disulfiram on the secretion and irrigation of an isolated and denervated gastric pouch was studied in four male mongrel dogs weighing 13 to 16 kg. The operation was performed 4 weeks prior to measurements. There were four treatments: control, 1 g/kg ethanol by stomach tube, 500 mg disulfiram orally, and disulfiram plus ethanol. Measurements made were: free acidity and total acidity, proteolytic activity, and gastric mucosal blood flow. Ethanol

caused an increase in gastric secretion and an increase in gastric mucosal blood flow. Disulfiram had no effect on volume or acidity of secretion, but inhibited the increase in proteolytic activity induced by ethanol. By itself, disulfiram had no effect on proteolytic activity. Disulfiram potentiated the effect of ethanol on gastric mucosal blood flow, but had no effect alone. Gastric hyperirrigation might lead to an increase in gastric ethanol absorption. 14 references.

001271 Lapin, I. P.; Oksenkru, G. F.; Ryzhov, I. V.; Nikiforov, V. A. Leningradskogo nauchno-issledovatel'skogo psikhonevrologicheskogo instituta im. V. M. Bekhtereva, Leningrad, USSR /Potentiation of reserpine action in frogs as a characteristic effect of antidepressants./ Potentsirovaniye deystviya rezepina na lyagushku kak kharakternyy effekt antidepressantov. Farmakologiya i Toksikologiya (Moskva). 6:144-147, 1976.

In a study of the mechanism of action of antidepressants the antidepressant thymonaleptics chlorimipramine, amitriptyline, and melitrace were found to potentiate the inhibitory effects of reserpine in 54 series of experiments with 2981 frogs to a greater degree than did antidepressants with less marked thymonaleptic action. Lu-5-003, azaphen, quipazine and desipramine, and also neuroleptics (promazine, stelazine and haloperidol), cholinolytics (atropine and benecytizine) and a stimulator (phenamine), were tested. The potentiating action of the tertiary amines imipramine, amitriptyline and protixen, was stronger than that of the corresponding secondary amines, desipramine, norprotixen and nortriptyline. Phenothiazines with the chlorine atom of the second position (chlorprotixen and chlorpromazine) potentiated the effect of reserpine less intensively than did their chlorine free analogs protixen and promazine. 14 references. (Author abstract modified)

001272 Lapin, Izyaslav; Jagiello-Wojtowicz, Ewa. Zaklad Farmakologii Instytutu Patologii Klinicznej Akademii Medycznej, Jaczewskiego 8, 20-090 Lublin, Poland Kynurenines antagonism against 5-HTP-potentiated action of imipramine and amitriptyline in frogs. Acta Physiologica Polonica (Warszawa). 27(6):591-594, 1976.

The effect of seven kynurenines (endogenous products of tryptophan metabolism) on the 5-hydroxytryptophan (5-HTP) potentiated action of imipramine and amitriptyline was studied in frogs. Imipramine plus 5-HTP and amitriptyline plus 5-HTP caused disappearance of the righting reflex in frogs. This effect was abolished by kynurenine, 3-hydroxyanthranilic acid, anthranilic acid, xanthurenic acid, picolinic acid, quinolinic acid, and nicotinic acid. Only nicotinic acid significantly reduced the characteristic tremor of the extremities induced by the antidepressant/5-HTP combination. (Author abstract modified)

001273 Lassen, J. Buus; Squires, R. F. Research Laboratories, A/S Ferrosan, Sydmarken 1-5, DK-2860 Soeborg, Denmark Potentiation of nialamide-induced hypermotility in mice by lithium and the 5-HT uptake inhibitors chlorimipramine and FG 4963. Neuropharmacology (Oxford). 15(11):665-668, 1976.

The effect of nialamide on motility of mice kept in a familiar cage was investigated. Fifty and 100 mg/kg nialamide administered subcutaneously produced only weak hypermotility, while 200 mg/kg nialamide elicited strong and long-lasting hypermotility consisting of continuous jerky locomotion, head movements, and tremor. The effect of 100 mg/kg nialamide was strongly potentiated by oral pretreatment with lithium chloride, chlorimipramine, and FG 4963. Nialamide and FG 4963 com-

bined produced a more prolonged hypermotility than chlorimipramine nialamide combination. Pretreatment with the 5-hydroxytryptamine synthesis inhibitor, p-chlorophenylalanine abolished potentiation of nialamide by lithium ion and reduced potentiation by chlorimipramine and FG 4963, indicating an involvement of 5-hydroxytryptamine. Nialamide plus L-tryptophan induced moderate, short lasting hypermotility, which was potentiated by chlorimipramine and FG 4963 but not by lithium ion, which suggests that lithium may act by increasing the concentration of L-tryptophan in brain. 27 references. (Author abstract)

001274 Le Bars, D.; Guilbaud, G.; Jurna, I.; Besson J. M. I.N.S.E.R.M. Groupe de recherche de neurophysiologie pharmacologique, 2 rue d'Alesia, F-75014 Paris, France *Differential effects of morphine on responses of dorsal horn lamina V type cells elicited by A and C fibre stimulation in the spinal cat.* Brain Research (Amsterdam). 115(3):518-524, 1976.

The effects of morphine upon responses elicited by the stimulation of large and small diameter afferent fibres on individual convergent dorsal horn units were studied to extend previous studies on lamina V type cells of the spinal cat. The results confirm a direct spinal level depressive action of morphine and morphine like agents. The existence of specific opiate receptors in the dorsal horn also supports this conclusion. Knowing the role of small diameter afferent fibres in the process of pain perception, the preferentially depressive effects of morphine on responses to activity in small afferent fibres could explain, to some extent, the analgesic properties of this drug. Moreover, these are specific effects immediately reversed by the administration of the opiate antagonist naloxone. The depressive effect of morphine must not be due to a peripheral site of action as the central action of opiate analgesic is well established. The different effects observed on responses evoked on the same cell by different groups of fibres could suggest a presynaptic site of action already proposed by different authors. 22 references.

001275 Le Bars, D.; Menetrey, D.; Besson J. M. Laboratoire de Physiologie des Centres nerveux, Université Pierre et Marie Curie, 4, avenue Gordon-Bennett, F-75016 Paris, France *Effects of morphine upon the lamina V type cells activities in the dorsal horn of the decerebrate cat.* Brain Research (Amsterdam). 113(2):293-210, 1976.

The effects of morphine (2mg/kg i.v.) upon the transmission of nociceptive messages at the spinal level was investigated in decerebrate cats by studying its effects on the activities of lamina V dorsal horn interneurons. In contrast to previous results obtained on the spinal cat, morphine had little or no effects on lamina V type cells in the decerebrate preparation. The mean values for spontaneous activity and responses to natural noxious stimulation were practically identical before and after morphine administration. Additional experiments using reversible spinalization (by cooling the cord at the thoracic level) suggest that the lack of effect of morphine on decerebrate animals could be explained by the fact that in this preparation, descending inhibitory influences are strongly exacerbated and thus may mask the depressive effects of this drug. These results indicate that the direct electrophysiological evidence of an increase of the descending control systems after morphine administration must be performed in the contact preparation in order to avoid the effects of their exacerbation in the decerebrate state. 63 references. (Journal abstract modified)

001276 Leifer, Marvin W.; Bridger, Wagner H. Dept. of Psychiatry, Albert Einstein College of Medicine, Bronx, NY *Effects of mescaline on flinch and movement shock thresholds in rats.* Biological Psychiatry. 11(4):457-461, 1976.

To test the hypothesis that frequently observed effects of mescaline on aversive conditioning might be mediated through its effects on shock threshold, the effects of mescaline on shock threshold were investigated in rats. Either mescaline or saline solution was administered 10 minutes before testing to 18 rats, and all rats received 10 series of 15 shocks, each of progressive severity. Flinch, vocalization, and movement responses were measured as indicators of shock threshold. Results indicate that mescaline had a small but significant effect in raising flinch and vocalization responses, and that it insignificantly demonstrated a trend toward raising the movement threshold. It is concluded that any contribution of this shock threshold effect to mescaline induced excitation in aversive conditioning is likely to be small. A brief discussion of mescaline's excitatory effect on behavior in the aversive conditioning paradigm is presented. 26 references.

001277 Lichtensteiger, Walter; Felix, Dominik; Lienhart, Ruth; Hefti, Franz. Institute of Pharmacology, University of Zurich, CH-8006 Zurich, Switzerland *A quantitative correlation between single unit activity and fluorescence intensity of dopamine neurons in zona compacta of substantia nigra, as demonstrated under the influence of nicotine and physostigmine.* Brain Research (Amsterdam). 117(1):85-103, 1976.

In order to investigate the possible relationship between neuronal activity and cellular fluorescence intensity, extracellular recordings of single unit activity and determinations of fluorescence intensity of dopamine (DA) neurones by histochemical microfluorimetry were performed in the same (rostral) part of zona compacta of substantia nigra in male rats. In urethane anaesthesia, zona compacta neurones characteristically showed a slow and fairly regular type of firing. Nicotine induced a transient decrease in unit activity for 1 min followed by a sustained increase in firing rate. Microfluorimetric examination of the fluorescence intensity developed at the end of the 30 min observation period by the DA neurons of the same area revealed a marked rise in cellular fluorescence intensity. Release of DA from terminals was indicated by an increase in homovanillic acid concentration of caudate putamen in rats subjected to the same nicotine treatment. When tested on one cell during a prolonged period of time, physostigmine caused an initial increase in firing rate of zona compacta neurones followed by a decrease of unit activity. In agreement with previous observations in mice, fluorescence intensity of nigral DA neurones likewise showed a biphasic change with an initial rise and subsequent decrease. When mean unit activity and mean fluorescence intensity of individual rats out of the various experimental groups were related to each other, a highly significant positive correlation between neuronal fluorescence intensity and firing rate was found. These findings indicate that cellular fluorescence intensity of DA neurone groups can be used as an index of the level of neuronal activity, except for cases where a drug treatment interferes directly with catecholamine synthesis or storage mechanisms. 34 references. (Author abstract modified)

001278 Lien, E. L.; Fenichel, R. L.; Garsky, V.; Sarantakis, D.; Grant, N. H. Research Division, Wyeth Laboratories, Philadelphia, PA 19101 *Enkephalin-stimulated prolactin release.* Life Sciences (Oxford). 19(6):837-840, 1976.

The effect of methionine-enkephalin and leucine-enkephaline on prolactin secretion was studied in vivo and in vitro in a

study of morphine mediated activities. Administration of methionine-enkephalin to rats resulted in a consistent increase in plasma prolactin. In monolayer cultures of rat pituitaries both enkephalins released prolactin at low concentrations. A significant rise in prolactin levels was seen by either subcutaneous or intravenous routes. The inhibition of enkephalin stimulated prolactin release by naloxone was also demonstrated, but no effect of either naloxone or somatostatin on basal prolactin release was observed. Results are in agreement with previous findings that methionine-enkephalin has more pronounced effects in binding to opiate receptors, suggesting a direct effect of the enkephalins on the pituitary in addition to any central nervous system activities of these compounds. Methionine-enkephalin, in addition to its analgesic properties, may be an endogenous prolactin releasing hormone. 8 references. (Author abstract modified)

001279 Lippmann, W.; Pugsley, T. A. Department of Biochemical Pharmacology, Ayerst Research Laboratories, Montreal, Quebec, Canada H3C 3J1 **Effects of viloxazine, an antidepressant agent, on biogenic amine uptake mechanisms and related activities.** Canadian Journal of Physiology and Pharmacology (Ottawa). 54(4):494-509, 1976.

The effects of viloxazine, a clinically effective antidepressant, on noradrenaline (NA) and 5-hydroxytryptamine (5-HT) uptake and various related pharmacological activities were determined and compared to those of the tricyclic antidepressants desimipramine, imipramine, and amitriptyline. Viloxazine inhibited 3H-NA uptake in the mouse and rat heart, being maximally about one half as potent as imipramine with a similar onset, but shorter duration of action than imipramine. The drug did not inhibit 3H-NA uptake in rat medulla or hypothalamus in contrast to desimipramine and imipramine, but it did alter 3H-NA metabolites in a similar manner. Viloxazine, like desimipramine, was a weak blocker of mouse brain 5-HT uptake, but differed from desimipramine as it potentiated 5-HT mediated functions in the mouse and rat, as did imipramine and amitriptyline, the latter drugs being relatively potent blockers of 5-HT uptake. Viloxazine potentiated the L-DOPA behavioral syndrome in the mouse, antagonized reserpine induced ptosis and hypothermia in the mouse, and inhibited gastric acid secretion in the rat, but was less potent than the tricyclic antidepressants. Like imipramine, the drug potentiated the ocular effects of L-adrenaline in the rabbit. It was similar to imipramine in potency in potentiating the apomorphine induced gnawing in the mouse. The drug antagonized oxotremorine induced hypothermia in the mouse but differed from the tricyclic antidepressants in not exhibiting the anticholinergic effects of blocking the tremors, salivation and lacrimation. Thus, viloxazine exhibits activities related to the biogenic amines both similar to and different from the tricyclics. These actions appear to be of relevance with respect to the antidepressant action of this drug. 61 references. (Author abstract)

001280 Liu, Shean-Jang; Wang, Richard I. H. Clinical Pharmacology 116E, Veterans Administration Center, Wood, WI 53193 **Enhanced development of tolerance to pentobarbital by desipramine inhibition of pentobarbital metabolism.** Biochemical Pharmacology (Oxford). 25(19):2211-2214, 1976.

The effect of tricyclic antidepressants on the development of tolerance to phenobarbital (PB) was studied using desipramine (DMI) as a model of a drug that interacts with PB. The development of tolerance to PB was assessed by comparing the sleeping times of drug treated and saline treated rats. The criterion of tolerance to PB was either a significant

reduction of sleeping time or a significant increase in enzyme activity. Two experiments were performed to assess the influence of DMI on the development of tolerance to PB. The enhanced development of tolerance to PB by subacute treatment with DMI and PB was indicated by the fact that rats pretreated with DMI plus PB had substantially higher PB hydroxylase activity than rats receiving PB alone. Rats pretreated with DMI alone or DMI plus PB gained less body weight at the end of the experiment than those rats pretreated with saline or PB alone. It is concluded that the effects of DMI and possibly other tricyclic antidepressants on PB action depend on the interval between the administration of DMI and PB. Acute treatment with DMI may potentiate the effect of PB after administration of DMI to acute and chronic PB treated rats. DMI may shorten the effect of PB after clearance of DMI from rats treated chronically with a combination of DMI and PB. The extrapolation of these findings to man would indicate that it is important to regulate the dose of PB according to the time of tricyclic antidepressant intake. 11 references.

001281 Logan, J. G.; O'Donovan, D. J. Department of Physiology, University College, Galway, Ireland **The effects of ouabain and the activation of neutral membrane ATPase by biogenic amines.** Journal of Neurochemistry (Oxford). 27(1):185-189, 1976.

The following hypotheses are examined: 1) the Mg ATPase of synaptic vesicles is activated by noradrenaline (NA) and 5-hydroxytryptamine (5-HT); 2) the existence of a ouabain insensitive ATPase activated by NA; and 3) NA antagonizes the inhibition of the (Na⁺-K⁺) ATPase by ouabain. The effects of M-noradrenaline (NA), 5-hydroxytryptamine (5-HT) and dopamine (DA) on the activities of Na⁺-K⁺ ATPase were studied in synaptic membranes from six regions of the rabbit brain. NA and 5-HT stimulated the synaptic membrane Na⁺-K⁺ ATPase from the cerebrum, but none of the amines influenced the activity of this enzyme in the other regions. The cortex synaptic membrane (Na⁺-K⁺)ATPase is postulated to have a direct role in the uptake of the biogenic amines. An indirect role is proposed for this enzyme in amine uptake into brain stem. 14 references. (Author abstract modified)

001282 Lopatka, J. E.; Brewerton, C. N.; Brooks, D. S.; Cook, D. A.; Paton, D. M. Dept. of Pharmacology, Univ. of Alberta, Edmonton, Alberta T6G 2H7, Canada **The protective effects of methysergide, 6-hydroxydopamine and other agents on the toxicity of amphetamine, phentermine, MDA, PMA, and STP in mice.** Research Communications in Chemical Pathology and Pharmacology. 14(4):677-687, 1976.

The effects of pretreatment with various agents (phentermine, 6-hydroxydopamine, methysergide, 4-chloroamphetamine, practolol, and haloperidol) on the lethal effects in mice of (plus)-amphetamine and (-)-amphetamine, phentermine, 4-methoxyamphetamine (PMA), 3,4-methylenedioxymphetamine (MDA), and 2,5-dimethoxy-4-methylamphetamine (STP) were studied with a view to determining the mechanisms responsible for their toxicity. The lethal effects of PMA and MDA were reduced by pretreatment with phentolamine and 6-hydroxydopamine suggesting that release of norepinephrine from peripheral adrenergic nerves contributed to their toxicity. Pretreatment with methysergide reduced the lethal effects of (plus)-amphetamine, (-)-amphetamine, MDA, PMA, and STP suggesting that an action on serotonergic receptors contributed to their toxicity. Pretreatment with 4-chloroamphetamine, practolol and haloperidol did not alter the lethal effects of the agents studied. 21 references. (Author abstract)

001283 Lorens, Stanley A. Department of Pharmacology, University of Bergen, MFH-Bygget, N-5000 Bergen, Norway **Comparison of the effects of morphine on hypothalamic and medial frontal cortex self-stimulation in the rat.** *Psychopharmacology* (Berlin). 48(2):217-224, 1976.

The effect of morphine on medial frontal cortex (MF) and hypothalamic self-stimulation (SS) was determined. Morphine suppressed SS responding or enhanced SS responding as a function of dose, time after injection, and the site stimulated. The MF SS groups were less sensitive to the toxic effects of morphine, and evidenced elevated rates of responding earlier after injection than the hypothalamic animals. The dose/response relationship of the MF rats, clearly differed from that of the hypothalamic rats. With repeated administration, tolerance developed rapidly to the suppressive effect, while the excitatory effect appeared earlier and tended to be enhanced. These data provide additional evidence against the hypothesis that the effect of morphine on SS behavior is non-specific. It is suggested that the excitatory effect is not dependent on the depressant effect and, therefore, probably is not a rebound phenomenon. It is also suggested that the toxic effects of morphine can either mask or delay the appearance of its facilitatory action on SS responding. 18 references. (Author abstract modified)

001284 Lullmann-Rauch, Renate. Department of Anatomy, University of Kiel, Olshausenstr. 40-60, D-2300 Kiel, Germany **Retinal lipidosis in albino rats treated with chlorphentermine and with tricyclic antidepressants.** *Acta Neuropathologica* (Berlin). 35(1):55-67, 1976.

This ultrastructural study was focused mainly on the effects, upon pigment epithelium, of several drugs that are thought to interfere with the enzymatic degradation of phospholipids. Albino rats received high oral doses of chlorphentermine, iprindole, 1-chloroamitriptyline, imipramine, or clomipramine. After treatment for several weeks the pigment epithelial cells were doubled in height due to deposition of excessive amounts of abnormal cytoplasmic inclusions which had a crystalloid substructure. Such inclusions which are known from previous studies to be associated with drug induced phospholipid storage are suggested to contain nondigestible phospholipids, which in pigment epithelium originate mainly from phagocytosed outer segment discs. The alterations were reversible by withdrawal of the drugs. The functional implications of the epithelial alterations remain to be elucidated. Additional examination of the neuroretina revealed numerous abnormal inclusions, mainly of multilamellated structure. Ganglion cells were affected most. The neuroretinal alterations were reminiscent of those described in human cases of inherited lipidoses. 37 references. (Author abstract)

001285 Magnuson, Debra J.; Tadeusik, Carol J.; Reid, Larry D. Bradley University, Peoria, IL 61606 **Addictive agents and intracranial stimulation: self-stimulation under morphine, amphetamine, and chlorpromazine.** *Bulletin of the Psychonomic Society*. 8(6):459-462, 1976.

Differential changes in self-stimulation in subjects having sustained high intensity intracranial stimulation were investigated with administration of morphine, amphetamine, and chlorpromazine. Rats were fixed with chronically indwelling electrodes for intracranial stimulation of the hypothalamus. Rats were exposed to varying levels of intracranial stimulation and pressed daily for the experience, with exposure to higher levels of intracranial stimulation reducing pressing behavior previously sustained by lower intracranial stimulation. After administration of the drugs it was noted that amphetamine and

morphine produced average increments in pressing at a nonreliable incidence, while chlorpromazine produced reliable decreases in bar pressing. Differential drug effects were not substantiated due to individual animal responses and variable responses across test groups. 12 references. (Author abstract modified)

001286 Maj, J.; Sarneck, J.; Klimek, V.; Rawlow, A. Institute of Pharmacology, Polish Academy of Sciences, 31-344 Cracow, Poland **On the anticataleptic action of cyproheptadine.** *Pharmacology Biochemistry and Behavior*. 5(2):201-205, 1976.

The anticataleptic action of cyproheptadine in comparison to that of atropine, promethazine, imipramine, desipramine, chlorimipramine, and nomifensine was studied in rats. The catalepsy induced by spiperone, pimozide, or fluphenazine was antagonized by cyproheptadine, atropine, and promethazine. Imipramine and nomifensine were less active; desipramine and chlorimipramine were without effect. Reserpine induced catalepsy and alpha-methyltyrosine induced catalepsy were counteracted by cyproheptadine, promethazine, and nomifensine, but not by atropine or tricyclic antidepressants. Only cyproheptadine and promethazine antagonized the catalepsy caused by a combined treatment with reserpine and alpha-methyltyrosine. Pilocarpine induced catalepsy was abolished by atropine, promethazine, and nomifensine and unaffected by tricyclic antidepressants. Atropine and promethazine also antagonized physostigmine induced catalepsy. The catalepsy induced by both cholinomimetic drugs was not changed or increased by cyproheptadine. It is suggested that cyproheptadine differs in its anticataleptic activity from all the drugs used for comparison. Possible mechanisms of this activity are discussed. 23 references. (Author abstract modified)

001287 Majchrowicz, Edward; Hunt, Walter A.; Piantadosi, Claude. Laboratory of Alcohol Research, National Inst. on Alcohol Abuse and Alcoholism, St. Elizabeth's Hospital, Washington, DC 20032 **Suppression by 1,3-butanediol of the ethanol withdrawal syndrome in rats.** *Science*. 194(4270):1181-1182, 1976.

A compound of low toxicity, 1,3-butanediol was tested for its ability to suppress an ethanol withdrawal syndrome. Male Sprague-Dawley rats were rendered physically dependent on ethanol by intragastric administration of ethanol at a dosage of 9 to 15 gms/kg per day over a 4 day period. A nonintoxicating oral dose of 1,3-butanediol at 4 gms/kg administered after elimination of ethanol from the blood was effective against the tremulous and convulsive components of the ethanol withdrawal syndrome in all animals for 1 to 5 hours. This period coincided with the time of maximum severity of the withdrawal syndrome, as seen in the control animals. (Author abstract)

001288 Mannisto, P. T.; Saarnivaara, L. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10 A, SF-00170, Helsinki 17, Finland **Effects of lithium and rubidium on the antinociception and behaviour in mice: II. Studies on three tricyclic antidepressants and pimozide.** *Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 222(2):293-299, 1976.

The effects of lithium chloride (LiCl) and rubidium chloride (RbCl) on the antinociception caused by three antidepressants and pimozide were studied in mice. On the hot plate LiCl given acutely or chronically did not modify the antinociception of any drug, although it augmented hypothermia induced by chlorimipramine and occasionally also caused definitive changes in motor abilities. In the phenyl writhing test LiCl

when given for 21 days, enhanced the nearly complete antinociception caused by chlorimipramine, doxepine, and pimo-
zide. The effects of the ions did not seem to be related to
change in body temperature, motor coordination or motility. 20
references. (Author abstract modified)

001289 Mantle, T. J.; Houslay, M. D.; Garrett, N. J.; Tipton, K. F. Department of Biochemistry, Tennis Court Road, Cambridge CB2 1QW, England **5-Hydroxytryptamine is a substrate for both species of monoamine oxidase in beef heart mitochondria.** *Journal of Pharmacy and Pharmacology* (London). 28(9):667-671, 1976.

The activity of beef heart mitochondrial monoamine oxidase towards 5-hydroxytryptamine (5-HT) is inhibited by the selective inhibitors clorgyline, PCO (5-phenyl-3-(N-cyclopropyl)-ethylamine-1,2,4-oxadiazole) and Deprenyl with a biphasic dependence on the inhibitor concentration. The activities towards tyramine, dopamine and tryptamine were also inhibited in a biphasic manner, but the apparent proportions of the two enzyme species active on dopamine and tryptamine depended on the inhibitor used. Phenethylamine oxidation was inhibited in a monophasic manner suggesting that only a single enzyme species was responsible for the oxidation of this substrate. The biphasic response of 5-HT oxidation to inhibition by clorgyline persisted when functionally competent mitochondria were used and was unaffected by the soluble amine oxidase inhibitors semicarbazide and aminoguanidine. These results indicate that the behavior of the beef heart enzyme towards selective inhibitors is considerably different from that of any preparations previously studied and suggest that the classification of monoamine oxidase activities into A and B types may be only of limited usefulness. 25 references. (Journal abstract)

001290 Marcy, R.; Quermonne, M. A. Department of Pharmacology, University of Caen Pharmaceutical Unit, 14032 Caen Cedex, France **Decremental skin conductance response in mice, during iterative photostimulation; an attention-sustaining capacity model for psychopharmacological research.** *British Journal of Pharmacology* (London). 58(3):437P-438P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the possibility of using an alteration of decreased skin conductance reaction (SCR) to iterative photostimulation as a means of studying psychopharmacological drugs. Repeated presentation of an attention getting stimulus caused a decrement and eventual extinction of the SCR. It has been demonstrated that psychoanaleptics delay SCR extinction, while central nervous system depressants speed it up. Amphetamine and related compounds caused a delay of SCR extinction. Unexpectedly, fenfluramine and piracetam also caused a delayed SCR extinction although neither drug has any stimulant properties that are known. The measurement of the delay or increase in SCR extinction during monotonous stimulation may serve as a model for attention sustaining capacity under the effect of drugs, since it is not exclusively influenced by drugs modifying general activity but seems sensitive to specific central effects not readily demonstrable otherwise. 2 references.

001291 Marczyński, Thaddeus J.; Hackett, John T. Department of Pharmacology and Psychiatry, University of Illinois Medical Center, Chicago, IL 60612 **Dose-dependent dual effect of morphine on electrophysiologic correlates of positive reinforcement (reward contingent positive variation: RCPV) in the cat.** *Pharmacology Biochemistry and Behavior*. 5(2):95-105, 1976.

The postreinforcement electroencephalographic (EEG) synchronization (PRS) and the associated epicortical steady potential shift (reward contingent positive variation: RCPV) restricted to the occipital cortex were studied in cats trained to press a lever for milk reward. Low doses of morphine cause a strong monophasic enhancement of PRS/RCPV. Larger doses of morphine have a biphasic effect. The initial enhancement of PRS/RCPV responses is followed by a strong suppression of PRS/RCPV responses. Chlorpromazine promptly restores the EEG responses. During the peak effect of morphine induced enhancement, the reward related EEG effect also occurs prior to a nonrewarded bar-press. The dissociation of the PRS/RCPV from consumption is much more conspicuous in animals having a high baseline frequency of PRS oscillations and in whom morphine produced a more significant slowing. Unlike LSD-25, morphine does not restore the reward induced phenomena in darkness. 31 references. (Author abstract modified)

001292 Marsden, C. A.; Curzon, G. Department of Neurochemistry, Institute of Neurology, Queen Square, London WC1 3BG, England **Effects of altered brain 5-hydroxytryptaminergic activity on brain tryptophan, 5-hydroxytryptamine and 5-hydroxyindoleacetic acid.** *Neuropharmacology* (Oxford). 15(11):703-708, 1976.

The effects of procedures known to alter 5-hydroxytryptaminergic activity (raphe stimulation, raphe lesions and exposure to elevated temperature) on brain tryptophan, 5-hydroxytryptamine (5-HT), and 5-hydroxyindoleacetic acid (5-HIAA) concentrations were investigated. Electrical stimulation of the dorsal raphe nucleus of unanaesthetized unretrained rats for 1 hour, using implanted electrodes, significantly increased (5-HAA) concentrations in the hypothalamus, striatum, midbrain, and cortex but not in the hippocampus. The level of 5-HT fell proportionately with the rise of (5-HIAA) in the midbrain but did not alter significantly in any other region. Tryptophan concentration was not significantly altered except in the hypothalamus where it increased moderately. Rats kept at 40 degree C for 60 minutes had significantly increased plasma, and brain tryptophan and brain 5-HIAA. Lysergic acid diethylamide prevented only the increase in acid. Electrolytic lesions in the dorsal and median raphe nuclei markedly lowered brain 5-HT and 5-HIAA but had no effect on brain or plasma tryptophan. Therefore, evidence is against a major role for brain tryptophan changes in the regulation of 5-HT synthesis following alteration of 5-HT activity. Other possible factors involved in the relationship of 5-HT metabolism to neuronal activity are discussed. 28 references. (Author abstract)

001293 McLennan, H.; Wheal, H. V. Department of Physiology, University of British Columbia, Vancouver, BC V6T 1W5, Canada **The specificity of action of three possible antagonists of amino acid-induced neuronal excitations.** *Neuropharmacology* (Oxford). 15(11):709-712, 1976.

The actions of three compounds, glutamic acid diethylester, 1-hydroxy-3-aminopyrrolidone-2, and L-5,6-dimethoxyaporphine (nuciferine) which have been claimed to be antagonists of excitatory amino acid and particularly of glutamate excitations of central neurones, were compared in the rat and the cat. Suitable electrophoretic "doses" of glutamic acid diethylester antagonized the effects of glutamate and aspartate to a much greater extent than those of homocysteate or acetylcholine. 1-Hydroxy-3-aminopyrrolidone-2 distinguished between glutamate/aspartate and homocysteate but not acetylcholine. Nuciferine showed no selectivity among the amino acids. Large applications of any of the compounds

would, however, antagonize the effects of all of the excitatory agonists. 17 references. (Author abstract)

001294 Meldrum, B. S.; Smyth, M. R.; Franklin-Smyth, W.; Clifford, J. M. Department of Neurology, Institute of Psychiatry, Denmark Hill, London, England **The relationship between the anticonvulsant properties of SC-13504 and its plasma levels, measured by polarography, in baboons with photosensitive epilepsy.** *Psychopharmacology* (Berlin). 51(1):59-64, 1976.

Plasma levels of SC-13504 were determined by differential pulse polarography after intravenous administration to baboon (*Papio papio*) with photosensitive epilepsy and correlated with behavioral changes and the anticonvulsant action of the drug. Protection against photically induced seizures or self-sustaining myoclonic responses occurred 30 min to 120 min after 4mg/kg to 8mg/kg doses of SC-13504 (when plasma levels were 1mg/ml or greater). Mild, transient sedation was the only side-effect occurring with the lower doses, but the 8mg/kg dose produced severe sedation, nystagmus, reduction of muscle tone, closure and tremor of the eyelids, reductions in aggressiveness and spontaneous movement, and electroencephalographic changes indicative of toxicity. 14 references. (Author abstract modified)

001295 Mohler, H.; Patel, A. J.; Balazs, R. Medical Research Department, F. Hoffmann-La Roche and Co. Ltd., CH-4002, Basel, Switzerland **gamma-Hydroxybutyrate degradation in the brain in vivo: negligible direct conversion to GABA.** *Journal of Neurochemistry* (Oxford). 27(1):253-258, 1976.

The metabolism of gamma-hydroxybutyrate (GHB) was studied by following the fate of (1-14C)GHB in mouse brain after an intravenous injection. Cerebral uptake of GHB was rapid and this substance disappeared from brain tissue with a half-life of approx 5 min. Degradation of (1-14C)GHB took place in the brain since 14C was incorporated in amino acids associated with the tricarboxylic acid cycle: the labelling pattern was consistent with the oxidation of GHB via succinate through the cycle, rather than with beta-oxidation of GHB. Conversion of (14C)GHB into (14C)GABA prior to oxidation was negligible. It is concluded that it is unlikely that the pharmacological action of GHB would be mediated through GABA formation. 30 references. (Author abstract modified)

001296 Mora, F.; Phillips, A. G.; Koolhaas, J. M.; Rolls, E. T. Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford, OX1 3UD, England **Prefrontal cortex and neostriatum self-stimulation in the rat: differential effects produced by apomorphine.** *Brain Research Bulletin*. 1(5):421-424, 1976.

In a dose response experiment, the effects intraperitoneal injections of the dopamine receptor agonist, apomorphine were studied on self-stimulation elicited from electrodes implanted in the medial and sulcal prefrontal cortex and caudate-putamen in the rat. From the medial and sulcal prefrontal cortex electrodes, apomorphine produced a dose related decrease of self-stimulation rate which was consistent across animals. From the caudate-putamen electrodes, on the contrary, apomorphine produced a facilitatory effect in the majority of animals at one or more doses, however, at other doses a decreased self-stimulation rate was observed. The clear and consistent effects of apomorphine on self-stimulation of the prefrontal cortex, together with other experimental evidence in the same line, suggest that dopamine is mediating self-stimulation of this cortical area. 24 references. (Author abstract)

001297 Morgan, William W.; Grant, Roberta W. Department of Anatomy, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Increased rate of disappearance of serum probenecid in barbital dependent rats.** *European Journal of Pharmacology* (Amsterdam). 40(2):349-357, 1976.

The effects of chronic barbital administration on serotonin (5-HT) turnover were estimated in rats using the probenecid method and the effects of chronic barbital consumption on the metabolism of probenecid were investigated. A statistically significant decrease in 5-hydroxyindoleacetic acid (5-HIAA) accumulation occurred in the cerebral cortex, medulla/pons and midbrain of barbital treated animals. Gas chromatography revealed that serum probenecid levels were significantly lower in treated rats than in controls, while levels of a probenecid metabolite were significantly increased. It is suggested that the reduced accumulation of 5-HIAA in brain areas of barbital dependent rats is the result of the more rapid decline of probenecid rather than a true decrease in 5-HT turnover. 14 references. (Author abstract modified)

001298 Mosko, Sarah S.; Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Electrophysiological evidence against negative neuronal feedback from the forebrain controlling midbrain raphe unit activity.** *Brain Research* (Amsterdam). 119(2):291-303, 1976.

The hypothesis that the activity of serotonin (5-HT) containing neurons of the midbrain raphe is subject to negative neuronal feedback regulation was examined. The effect of complete transections of the neuraxis placed just rostral to the midbrain raphe nuclei on the efficacy of chlorimipramine and parachloroamphetamine, which elevate synaptic 5-HT, was investigated in rats. Such transections neither blocked nor attenuated the depressive effect of intravenously administered chlorimipramine or parachloroamphetamine on midbrain raphe unit discharge. It is suggested that neuronal feedback involving the forebrain does not mediate the depressive effect of drugs which elevate synaptic 5-HT on midbrain raphe neuronal activity. An action at serotonergic synapses intrinsic to the midbrain raphe is suggested as an explanation for the persistence of drug effects in transected animals. 54 references. (Author abstract modified)

001299 Mozhayeva, G. N.; Naumov, A. P.; Negulyayev, Yu. A. Institut tsytologii AN SSSR, Leningrad, USSR **Effect of anicotine on some properties of sodium channels in the Ranvier node membrane.** *Vliyanie akonitina na nekotorye svoystva natrievykh kanalov membrany perekhvata Ranv'ye.* *Neyrofiziologiya* (Kiev). 8(2):152-160, 1976.

The effect of anicotine on sodium channels in the Ranvier node membrane was studied in frogs. It was shown that anicotine causes the appearance of two types of modified channels in the membrane. The first channel type is activated by high negative potentials and is inactivated partially or not at all, while the second type loses conductivity in the course of anicotine action and its kinetic characteristics and area of activation are similar to those of ordinary sodium channels. The sensitivity of modified channels to tetrodotoxin remains at the same level as for ordinary sodium channels. 26 references. (Author abstract modified)

001300 Musty, Richard E.; Lindsey, Charles J.; Carlini, E. A. University of Vermont, Burlington, VT **6-Hydroxydopamine and the aggressive behavior induced by marihuana in REM sleep-deprived rats.** *Psychopharmacology* (Berlin). 48(2):175-179, 1976.

A study was carried out to determine the effects of 6-hydroxydopamine (6-OHDA), intraventricular injection of norepinephrine (NE) and intraventricular injection of dopamine (DA) on marihuana induced aggression in REM sleep deprived rats. 6-OHDA pretreatment increased the aggressive behavior induced by marihuana in REM sleep deprived rats. Brain catecholamine assays revealed that 6-OHDA depleted DA and NE to a different extent, increasing the DA/NE ratio. Intraventricular injection of NE significantly decreased the aggressive behavior of these animals, whereas control solution or DA injections had no effect. The possible role played by DA and NE in the aggressive behavior induced by marihuana in REM sleep deprived rats is discussed. 29 references. (Author abstract modified)

001301 Nahorski, S. R.; Rogers, K. J. Department of Pharmacology, School of Medicine, University of Leicester, University Road, Leicester LE1 7RH, England **Inhibition of 3',5'-nucleotide phosphodiesterase and the stimulation of cerebral cyclic AMP formation by biogenic amines in vitro and in vivo.** *Neuropharmacology* (Oxford). 15(10):609-612, 1976.

A number of compounds that have been shown to be potent inhibitors of phosphodiesterase in brain homogenates were examined for their ability to potentiate biogenic amine stimulated cyclic adenosine monophosphate (AMP) formation in mouse cerebral cortex slices and in chick cerebral hemispheres in vivo. Of the drugs examined, only 4-(3-butoxy-4-methoxy)-2-imidazolidinone (Ro20-1724) and 2-amino-6-methyl-5-oxo-4-n-propyl-4,5-dihydro-s-triazolo (1,5-a) pyrimidine (IC163197) significantly potentiated the cyclic AMP response to biogenic amines. Theophylline, papaverine and medazepam were ineffective both in vivo and in vitro. Histamine and dopamine were completely inactive in stimulating cyclic AMP formation in mouse cerebral cortex slices but in the presence of Ro20-1724 or IC163197, significant accumulations of the nucleotide were produced. Prostaglandin E-1 and 5-hydroxytryptamine did not enhance cyclic AMP formation either in the presence or absence of Ro20-1724. However, this phosphodiesterase inhibitor greatly potentiated the effect of adenosine. It is suggested that the discrepancy between the effects of drugs on phosphodiesterase in broken cell and whole cell preparations may be related to differential inhibition of different forms of phosphodiesterase in brain or to the relative lipophilic nature of the compounds examined. 21 references. (Author abstract modified)

001302 Nahorski, S. R.; Smith, Brenda M. Department of Pharmacology and Therapeutics, School of Medicine, University of Leicester, Leicester LE1 7RH, England **Characteristics and altered sensitivity of cerebral beta-adrenoceptors assessed by (3H)-propranolol binding.** *British Journal of Pharmacology* (London). 58(3):435P-436P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the characteristics and altered sensitivity of cerebral beta-adrenoceptors catecholamines in chick brain fractions by tritiated propranolol binding. Cyclic AMP formation stimulated by adrenaline, noradrenaline, and isoprenaline was antagonized by propranolol and was considerably more potent than the cardioselective beta1-adrenoceptor antagonists metoprolol and practolol. The results suggest that the beta-adrenoceptor in chick cerebral hemispheres resembles that found in bronchial and vascular smooth muscle (beta2) rather than in heart (beta1). Also suggested is that the loss of responsiveness of cerebral beta-adrenoceptors following chronic exposure to isoprenaline is associated with a loss of available receptor binding sites. 5 references.

001303 Naik, S. R.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Central GABA receptor agonists: comparison of muscimol and baclofen.** *Neuropharmacology* (Oxford). 15(8):479-484, 1976.

Using a number of criteria that have helped to characterize gamma-aminobutyric acid (GABA) receptor stimulation in the central nervous system, the actions of baclofen and muscimol were compared with those of diazepam and phenobarbital in the rat. The pharmacological profile of baclofen differs from that of a GABA agonist but in contrast many actions of muscimol may be a reflection of GABA receptor stimulation. These are: a selective antagonism against isoniazid seizures, a decrease in cerebellar guanosine 3,5 cyclic monophosphate (cyclic GMP) content and a selective antagonism against the increase in cerebellar cyclic GMP content elicited by isoniazid. This antagonism is elicited by muscimol doses that per se fail to lower the cyclic GMP content of cerebellum. Muscimol, which is structurally related to GABA, could be a candidate for studying the pharmacology and the therapeutic potentials of GABA receptor agonists. 38 references. (Author abstract modified)

001304 Nastuk, William L.; Su, Philip C.; Doubilet, Peter. Department of Physiology, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **Anticholinergic and membrane activities of amantadine in neuromuscular transmission.** *Nature* (London). No.1 5581:76-79, 1976.

Single cell electrophysiological techniques were used to study the action of amantadine on junctional and extrajunctional membranes in frogs. Results show that amantadine, in clinically effective concentrations, rapidly inhibits neuromuscular transmission, and, when applied over a longer period of time, the drug also exerts a substantial effect on the conductile membranes of muscle fibers. It is suggested that the beneficial effect of amantadine in parkinsonism may depend to some extent on the capacity of this drug to inhibit cholinergic transmission in certain neuronal circuits involved in the central control of muscular movement. 11 references.

001305 Nazaretyan, R. A.; Arutyunyan, L. G.; Arutyunyan, S. P.; Simonyan, I. M. *NII obshchey gigiyeny i professional'nykh zabolevaniy im. N. B. Akopyana, MZ Armyanskoy SSR., Yerevan, USSR /Disorder of cholinergic mediation under hyperthermic conditions and its experimental pharmacotherapy./ Narusheniya kholinergicheskoy meditsii v usloviyakh gipertermii i ikh eksperimental'naya farmakoterapiya. Zhurnal Eksperimental'noy i Klinicheskoy Meditsiny* (Yerevan). 16(4):38-42, 1976.

Effects of single and repeated exposure to high temperature external media on the acetylcholine content and choline esterase activity in tissues and blood were investigated in white rats. Results showed 2 phase change in the amount of acetylcholine, and suppression of choline esterase activity in different periods of an attack of hyperthermia. Pharmacotherapy with dibazol facilitated both prevention of these changes, and quick restoration of the disturbed relations between the mediator and the enzyme. 10 references.

001306 Nicholson, C.; Bruggencate, G. Ten; Senekowitsch, R. Division of Neurobiology, Department of Physiology and Biophysics, University of Iowa, Iowa City, IA 52242 **Large potassium signals and slow potentials evoked during aminopyridine or barium superfusion in cat cerebellum.** *Brain Research* (Amsterdam). 113(3):606-610, 1976.

The effects of application of 3-aminopyridine, 4-aminopyridine and barium to the cat cerebellum were investigated. Although aminopyridines block the repolarizing potassium flux of the neuronal action potential and barium also blocks potassium fluxes, application of these substances to the cat cerebellum enables a large transient extracellular potassium signal and a slow potential to be evoked by a single local surface stimulus. Possible mechanisms for these paradoxical findings are discussed. 18 references.

001307 Nickolson, Victor J.; Wolhuis, Otto L. Medical Biological Laboratory TNO, 139 Lange Kleiweg, ND-2100 Bijswijk, The Netherlands **Differential effects of the acquisition enhancing drug pyrrolidone acetamide (piracetam) on the release of proline from visual and parietal rat cerebral cortex in vitro.** Brain Research (Amsterdam). 113(3):616-619, 1976.

The effect of piracetam on the metabolism of proline was studied in rat cerebral cortex tissue slices in order to investigate the effects of the drug on information processing in the cerebral cortex. Piracetam decreases spontaneous proline release in the visual cortex and increases proline release in the parietal cortex. It is suggested that the facilitation of the visual evoked response and enhancement of acquisition of piracetam may be related to the effects of the drug on cortical proline metabolism. 13 references.

001308 Nickolson, Victor J.; Wolhuis, Otto L. Medical Biological Laboratory TNO, 139, Lange Kleiweg, Rijswijk 2100, The Netherlands **Protein metabolism in the rat cerebral cortex in vivo and in vitro as affected by the acquisition-enhancing drug piracetam.** Biochemical Pharmacology (Oxford). 25(20):2237-2240, 1976.

In a further investigation of the association of the consolidation of new information with the systems of cerebral problems, the effect of 2-pyrrolidone-N-acetamide (Piracetam) on rat cerebral protein metabolism was studied in vivo and in vitro. The drug was shown to stimulate the uptake of labeled leucine by cerebral cortex slices and has no effect on the incorporation of leucine into cerebral protein in tissue slices or in vivo, but inhibits the breakdown of newly formed protein in tissue slices. 14 references. (Author abstract modified)

001309 Nickolson, Victor J.; Wolhuis, Otto L. Medical Biological Laboratory TNO, 139, Lange Kleiweg, Rijswijk 2100, The Netherlands **Effect of the acquisition-enhancing drug piracetam on rat cerebral energy metabolism. Comparison with naftidrofuryl and methamphetamine.** Biochemical Pharmacology (Oxford). 25(20):2241-2244, 1976.

The effects of Piracetam, Naftidrofuryl, and methamphetamine on several parameters of cerebral energy metabolism were studied. Neither Piracetam nor Naftidrofuryl affected the cerebral contents of adenine nucleotides or the adenylate energy charge. Methamphetamine also had no effect on cerebral adenine nucleotides. Piracetam increased the activity of adenylate kinase in isotonicity diluted rat brain homogenates. It is concluded that although Piracetam has no effect on cerebral energy metabolism under normal conditions, it may have a beneficial effect under marginal conditions like those met during hypoxia. It is suggested that the adenylate kinase stimulating action is responsible for the protective effect of Piracetam against cerebral hypoxia. The adenylate kinase stimulating action may also be related to the enhancement of acquisition under training conditions where cerebral energy metabolism is disturbed. 20 references. (Author abstract modified)

001310 Nistico, G.; Gargiulo, G.; Rotiroli, D.; Preziosi, P. Veterinary Pharmacology, University of Messina, Messina, Italy **Acute central effects of 5,6-dihydroxytryptamine in fowl.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 222(2):267-271, 1976.

In adult hens infusion into the third cerebral ventricle of 5,6-dihydroxytryptamine (5,6-DHT) produced, after 5-10 min behavioral and electrocortical sedation and sleep lasting about 6-8 hr, and a monophasic or biphasic increase in body temperature for about 8 hr. It is concluded that behavioral and electrocortical effects evoked by 5,6-DHT seem to be due to a synergistic action of 5-hydroxytryptamine (5-HT) and catecholamines displaced and released by this compound, whereas hyperthermic effects seem to be due to a more sustained release of 5-HT and/or to a direct action on 5-HT receptors and/or inhibition of 5-HT reuptake. 17 references. (Author abstract modified)

001311 Noble, E. P.; Syapin, P. J.; Vigran, R.; Rosenberg, A. Division of Neurochemistry, Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA 92664 **Neuraminidase-releasable surface sialic acid of cultured astroblasts exposed to ethanol.** Journal of Neurochemistry (Oxford). 27(1):217-221, 1976.

Chronic exposure of intact cultured primary hamster astroblasts, clonal line NN, to 100 mM ethanol resulted in significant increases, 10 to 52% in the releasability of sialic acid from the cell by exogenously added Clostridium perfringens neuraminidase. The total cellular sialic acid content was independent of length of cell exposure to ethanol but varied with the age of the cells. These data suggest that exposure of cells for prolonged periods to ethanol results in steric modification of surface glycoproteins. 28 references. (Author abstract modified)

001312 Northup, L. R. Institute for Behavioral Genetics, University of Colorado, Boulder, CO 80309 **Additive effects of ethanol and Purkinje cell loss in the production of ataxia in mice.** Psychopharmacology (Berlin). 48(2):189-192, 1976.

In order to assess the contribution of cerebellar effects of ethanol to the production of ataxia, locomotor activity was tested after ethanol injections in a cerebellar mutant strain of mouse (suffering from loss of most of their cerebellar Purkinje cells) and in control mice. An additive effect of ethanol and cerebellar pathology in the production of ataxia was found. It is suggested that the transient elimination of Purkinje cell activity following an injection of ethanol is responsible for the additive effect. 7 references. (Author abstract modified)

001313 O'Dea, Robert F.; Zatz, Martin; Axelrod, Julius. Natl. Inst. of MH, LCS, Bldg. 10, 2D-47, Bethesda, MD 20014 **Catecholamine-stimulated cyclic GMP accumulation in the rat pineal: presynaptic site of action.** (Unpublished paper). Laboratory of Clinical Science, DCBR, IRP, NIMH.

The effects of several substances on accumulation of cyclic guanosine monophosphate (cGMP) in the rat pineal gland were investigated. Levonorepinephrine (NE) increased cGMP. The response consisted of two components. One component was stereospecific and inhibited by alpha-adrenergic antagonists while the other was not stereospecific and not readily inhibited by antagonists. Levoisoproterenol had a smaller effect and its action was not stereospecific. The stimulation of cGMP by these catecholamines was dependent upon extracellular calcium ion. Ouabain and potassium chloride produced a marked calcium dependent increase in pineal cGMP which was

blocked by phentolamine. Cholinergic agents did not stimulate cGMP. Surgical denervation of the pineal markedly reduced the cGMP response to levonorepinephrine, potassium chloride or ouabain but did not affect the response to levoisoproterenol. It is concluded that the data demonstrate the existence of a calcium dependent presynaptic mechanism for the generation of cGMP which may be mediated by an alpha-adrenergic like receptor. (Author abstract modified)

001314 Okamoto, K.; Quastel, D. M. J.; Quastel, J. H. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, B.C. V6T 1W5, Canada **Action of amino acids and convulsants on cerebellar spontaneous action potentials in vitro: effects of deprivation of Cl⁻, K⁺ or Na⁺. Brain Research (Amsterdam).** 113(1):147-158, 1976.

The variations in amino acid induced changes in discharge frequency of the spontaneous action potential exhibited by superfused guinea-pig cerebellar cortex slices produced by altering the ionic concentrations in the superfusion media were investigated. The manner in which strychnine, picrotoxin, and bicuculline affect the actions of amino acids in the frequency of spontaneous action potentials under different ionic conditions was also studied. Glycine, gamma-aminobutyric acid and beta-alanine cause inhibition of spontaneous action potentials by increasing chloride and potassium ion permeability. In a low chloride medium, the inhibition is converted to excitation. Glycine, taurine and beta-alanine, but not GABA, also affect permeability to sodium ion so that the excitatory effect of these compounds in low chloride media are greatly reduced by lowering the sodium content of the media. Excitation by GABA in low chloride media is abolished by picrotoxin and bicuculline. Inhibition by GABA in high chloride media is suppressed. Strychnine suppresses the effects of glycine, taurine and beta-alanine in high chloride media or in low chloride media. Bicuculline blocks the inhibitory effect of glycine, taurine and beta-alanine in high chloride media but does not affect their excitatory effects in a low chloride medium. 12 references. (Author abstract modified)

001315 Olney, John W.; Cicero, Theodore J.; Meyer, Edward R.; De Gubareff, Tasia. Department of Psychiatry, Washington University School of Medicine, St Louis, MO 63110 **Acute glutamate-induced elevations in serum testosterone and luteinizing hormone. Brain Research (Amsterdam).** 112(2):420-424, 1976.

The hypothesis that systemically administered glutamate (GLU) in doses too small to cause destruction of neurons in the arcuate nucleus of the hypothalamus might stimulate these neurons to fire at increased rates, thereby disturbing endocrine systems regulated by these neurons and producing changes in serum levels of testosterone and luteinizing hormone (LH), was investigated in male rats. Serum testosterone and LH increased 15 minutes after GLU administration, dropped to baseline levels by 30 minutes, then gradually rose again. Serum LH returned to near baseline levels by 6 hours but testosterone continued to rise, reaching a peak at 6 hours. The possible mechanisms by which GLU produces these effects are discussed. 22 references.

001316 Olney, John W.; Misra, Chandra H.; Rhee, Vesa. Department of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Brain and retinal damage from lathyrus excitotoxin, beta-N-oxalyl-L-alpha,beta-diaminopropionic acid. Nature (London).** 264(5587):659-661, 1976.

In a letter to the editor, a report is presented relating to an excitotoxin, beta-N-oxalyl-L-alpha,beta-diaminopropionic acid (ODAP), a neuroexcitatory amino acid isolated from the seeds of lathyrus sativus, which was administered intraperitoneally to immature mice, and which induces lesions in the retina, hypothalamus and lower medulla. This pattern of damage is similar to that demonstrated in animals after oral or subcutaneous administration of glutamate (Glu). The brainstem of mice treated with ODAP in this study was damaged at the level of the area postrema and the extent of damage to the brainstem was relatively greater for any given animal than the damage sustained in the hypothalamus. 17 references.

001317 Opitz, Klaus; Shafer, Genoveva. Institut für Pharmakologie und Toxikologie, Universität Münster, D-4400 Münster, FRG **The effect of lithium on food intake in rats. International Pharmacopsychiatry (Basel).** 11 (4):197-205, 1976.

The effect of lithium on the ingestive behavior and body weight of male and female Wistar rats was studied. Both single and repeated large intraperitoneally administered doses of lithium chloride in rats reduced food intake and water consumption. Small doses increased food intake and body weight during long-term treatment. With repeated doses the prompt anorexia and delayed polydipsia as well as weight loss were more pronounced in males than in female rats. The findings indicate that an increase in food intake may account for the increased body weight without recourse to the well known metabolic effects of lithium to account for weight gain. The sex differences in weight change may be accounted for by the sex differences in renal excretion of lithium. 33 references. (Author abstract modified)

001318 Organisciak, D. T.; Klingman, J. D. Department of Biological Chemistry, Wright State University, Col. Glenn Highway, Dayton, OH 45431 **Lithium induced alterations in rat ganglionic lipids. Brain Research (Amsterdam).** 115(3):467-478, 1976.

The effects of acute and chronic levels of lithium ion on the incorporation of (U-14C)-pyruvic acid into lipids of the rat superior cervical ganglion were determined. In control ganglia, sphingolipids contained 60% to 70% of the lipid radioactivity, glycerophospholipids 20% to 30% and neutral lipids 10% to 25%. Phosphatidylcholine contained 65%, of the glycerophospholipid label and 40% of the lipid phosphorus, while sphingomyelin contained 90% of the sphingolipid label and exhibited the highest specific activity over all. Cholesterol was the major neutral lipid. Ninety five percent of the glycerophospholipid label and 4% of the sphingomyelin label was localized in the fatty acids. The lipid and fatty acid compositions of all ganglia were similar. However the lipid radioactivity in chronic ganglia was lower than in control, with the sphingolipids most affected. In 80 minutes stimulated chronic ganglia stearic and oleic acid, radioactivity was depressed with respect to both control fatty acids and to the 14Cpalmitate of chronic tissues. In both chronic and acute lithium ganglia stimulated for 80 minutes, the specific activities of phosphatidylinositol were significantly lower than in control. In contrast to control, the labeling of sphingolipids in resting acute ganglia was higher than in stimulated tissues. 26 references. (Author abstract modified)

001319 Ozawa, Hikaru; Koide, Tohru. Department of Pharmacology, Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan **Pharmacodynamic actions of (S)-2 (4,5-dihydro 5-propyl-2(3H)-furylidene) 1,3-cyclopentanedione**

(oudenone). Japanese Journal of Pharmacology (Kyoto). 26(5):581-592, 1976.

The pharmacodynamic actions of (S)-2-(4,5-dihydro-5-propyl-2(3H)-furylidene)-1,3-cyclopentanedione (oudenone) were studied in both anesthetized animals and isolated organs. Oudenone induced an initial rise in blood pressure followed by a prolonged hypotension in the anesthetized rats. In unanesthetized spontaneously hypertensive rats (SHR), oudenone caused a dose related decrease in the systolic blood pressure. The initial pressor effect was diminished by pretreatments with phentolamine, guanethidine, hexamethonium and was abolished in the pithed rats. In addition, intracisternal administrations of oudenone showed a marked increase in blood pressure in the anesthetized rats, suggesting that the pressor effect may be due to centrally mediated actions. Oudenone, given intraarterially into the femoral artery, caused a long-lasting vasodilation in anesthetized dogs. At a relatively high dose, oudenone antagonized all pressor responses to autonomic agents and central vagus nerve stimulation in anesthetized rats and dogs. However, oudenone showed no anticholinergic, histaminergic, beta-adrenergic and adrenergic neuron blocking properties. The findings indicate that the initial pressor response of oudenone may have its origin in the central nervous system and that the hypotensive effect of oudenone is due to have a long lasting vasodilation and nonspecific effect on the responses to all the pressor substances. 22 references. (Author abstract)

001320 Pagel, John; Christian, S. T.; Quayle, E. S.; Monti, J. A. Neurosciences Program and Department of Psychiatry, University of Alabama in Birmingham, University Station, Birmingham, AL 35294 A serotonin sensitive adenylate cyclase in mature rat brain synaptic membranes. Life Sciences (Oxford). 19(6):819-824, 1976.

Production of cyclic adenosine 3',5'-monophosphate (cAMP) arising from 5-hydroxytryptamine (5-HT) interactions in rat synaptosomal membranes and indications of serotonin sensitive adenylate cyclase activity in adult rat brain are reported. The enzyme is localized in the synaptosomal plasma membrane and apparently has multiple activation sites for serotonin with specific activity maxima occurring at serotonin concentrations at low molar values. The production of cAMP at these sites appears to be unaffected by fluphenazine, while tryptamine, methysergide, and ergonovine decreased the stimulatory effect. It is concluded that the observed effects result from specific interactions of 5-HT with the adenylate cyclase present in rat brain synaptic membranes. 22 references. (Author abstract modified)

001321 Palmer, G. C.; Wagner, H. R.; Putnam, R. W. Department of Pharmacology, University of New Mexico, School of Medicine 915 Stanford Drive NE, Albuquerque NM 87131 Neuronal localization of the enhanced adenylate cyclase responsiveness to catecholamines in the rat cerebral cortex following reserpine injections. Neuropharmacology (Oxford). 15(11):695-702, 1976.

Rats were injected daily with reserpine for four days. The animals were sacrificed 4 hours subsequent to the last injection. Studies were performed as a means to determine alterations in catecholamine sensitivity of adenylate cyclase in the cerebral cortex following reserpine. In incubated tissue slices from reserpinized animals a greater accumulation of cyclic adenosine 3',5'-monophosphate (cyclic AMP) in response to norepinephrine and isoproterenol was seen. In control animals both alpha (phenolamine) and beta-blocking agents (propranolol) inhibited norepinephrine induced cyclic nucleo-

tide accumulation, while in the reserpine injected rats only propranolol was effective. The accumulation of cyclic AMP elicited by isoproterenol was inhibited by propranolol alone whether or not reserpine was administered. In cortical homogenates adenylate cyclase responsiveness to norepinephrine, isoproterenol, and dopamine was enhanced in animals pretreated with reserpine. An identical observation was found in isolated neuronal fractions, although increased sensitivity of the enzyme to dopamine was now absent. Neither alpha-blocking nor beta-blocking agents were effective in broken cellular preparations. These data are interpreted to suggest that following depletion of catecholamines by reserpine, the beta-receptor component of adenylate cyclase in the cortical neurones becomes hypersensitive to stimulation by catecholamines. 32 references. (Author abstract)

001322 Palmer, Gene C.; Manian, Albert A.; Sanborn, Carolyn R. Department of Pharmacology, University of New Mexico, School of Medicine, 915 Stanford Drive, N.E., Albuquerque, NM 87131 Effects of neuroleptic agents on cyclic GMP in rat cerebral cortex. European Journal of Pharmacology (Amsterdam). 38(1):205-209, 1976.

Cyclic guanosine 3',5'-monophosphate (cyclic GMP) levels were increased in incubated tissue slices from rat cerebral cortex in response to added cholinomimetic agents (carbachol and choline chloride) and neuroleptic compounds in a study of whether specific neuroleptic agents and respective derivatives would influence either the steady state levels of cyclic GMP or the increased accumulation of cyclic GMP in response to carbachol. The neuroleptic compounds used were chlorpromazine, 8-hydroxychlorpromazine, 7-hydroxychlorpromazine methiodide, haloperidol, thioridazine, chlorpromazine sulfoxide and promethazine. Calcium ion was required for this effect. Moreover, selected agents, namely 7,8-dihydroxychlorpromazine, 7,8-dimethoxychlorpromazine, chlorpromazine and clozapine, prevented the rise in cyclic GMP induced by carbachol. 13 references. (Author abstract modified)

001323 Pappas, Bruce A.; Saari, Matti; Peters, David A. V. Dept. of Psychology, Carleton University, Ottawa, Ontario, Canada Regional brain catecholamine levels after intraventricular 6-hydroxydopamine in the neonatal rat. Research Communications in Chemical Pathology and Pharmacology. 14(4):751-754, 1976.

Brain parts from 70-day-old rats which had been injected intraventricularly in the neonatal period with 6-hydroxydopamine (6-OHDA) were studied by fluorometric assay to determine regional brain catecholamine levels. The differences and similarities between the effects of intraventricular injection and reported effects of peripheral injection are discussed. The doses used in the intraventricular injections during the neonatal period severely depleted forebrain and diencephalic norepinephrine and striatal dopamine but increased pontine norepinephrine. 7 references.

001324 Paton, D. M. Department of Pharmacology, University of Alberta, Edmonton, Alberta T6G 2H7, Canada Effect of veratrine alkaloids on the efflux of extragranular noradrenaline from rabbit atria. Journal of Neurochemistry (Oxford). 27(5):1271-1272, 1976.

The effects of veratrine alkaloids on the efflux of extragranular radiolabeled noradrenaline (NA) were studied in atria isolated from reserpine pretreated rabbits. The veratrine alkaloids accelerated the efflux of radiolabeled NA from adrenergic nerves by a process that was not calcium ion dependent. This effect was apparently not due to exocytosis. The ef-

fect of the veratrine alkaloids on NA efflux was inhibited by tetrodotoxin, suggesting that the effect was dependent on the production of membrane depolarization. The ability of the veratrine alkaloids to accelerate NA efflux was also inhibited by cocaine and desipramine but not by lidocaine. Possible mechanisms by which the veratrine alkaloids may accelerate the efflux of extragranular NA are discussed. 13 references.

001325 Paton, D. M. Department of Pharmacology, University of Alberta, Edmonton, Alberta T6G 2H7, Canada **Effect of adrenergic neuron blocking agents and biguanides on the efflux of extragranular noradrenaline from adrenergic nerves in rabbit atria.** *Journal of Pharmacy and Pharmacology (London)*. 28(7):582-583, 1976.

The effects of adrenergic neuron blocking agents and related biguanides on the efflux of extragranular (-)(3H) noradrenaline were investigated in rabbit atria to further elucidate the structural requirements for acceleration of efflux. The effects on efflux of beta-phenethylamine, phenylethanolamine, and beta-hydroxyphenethylguanidine were also examined. Findings showed that potency was reduced by beta-hydroxylation and that it was markedly reduced from the guanidine substitution on the terminal nitrogen. The data demonstrate that adrenergic neuron blocking agents accelerate the efflux of (3H)noradrenaline located in the cytoplasm of adrenergic neurons, probably because the agents displace noradrenaline from postulated cytoplasmic binding sites for noradrenaline or by accelerative exchange diffusion. Neither a phenyl ring nor a terminal amino group separated from the ring by two carbon atoms was necessary for activity, since a variety of structures were capable of accelerating the (-)(3H) noradrenaline efflux. Possible explanations are offered for the unlikely finding that biguanides, metformin and phenformin, had no effect on efflux. 7 references.

001326 Paul, S. M.; Halaris, A. E.; Freedman, D. X.; Hsu, L. L. Department of Psychiatry, University of Chicago, 950 East 59th Street, Chicago, IL 60637 **Rat brain aryl acylamidase: stereospecific inhibition by LSD and serotonin-related compounds.** *Journal of Neurochemistry (Oxford)*. 27(2):625-627, 1976.

A study was conducted to examine the specificity of stereospecific inhibition of rat brain aryl acylamidase by lysergic acid diethylamide (LSD), and serotonin-related compounds. Homogenized rat brain was centrifuged and subjected to ammonium sulfate precipitation to obtain the enzyme for study. Enzymatic activity was assayed in an incubated mixture, and protein was determined and used for calculating specific activity. Results demonstrate that inhibition of rat brain aryl acylamidase occurs only in the presence of pharmacologically active tryptamine derivatives, is stereospecific with respect to its inhibition by LSD, and thus might provide a basis for studying LSD serotonin receptor interaction in vitro. 14 references.

001327 Pertschuk, Louis P.; Ford, Donald H.; Rainford, Evelyn A.; Brigati, David J. State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203 **Localization of phenobarbital in mouse central nervous system by immunofluorescence.** *Acta Neurologica Scandinavica (Kobenhavn)*. 53(5):325-334, 1976.

Through the use of antiepileptic serum in an indirect immunofluorescence system, phenobarbital was detected in the central nervous system of mice given an overdose of drugs. Localization was primarily within neurons of the limbic system, caudate nucleus, cerebellum, cervical spinal cord, and

trigeminal ganglion. This technique may be of value in acquiring additional information about the barbiturates as well as being of value to the forensic pathologist. 25 references. (Author abstract modified)

001328 Perumal, A. S.; Mahadik, S. P.; Rapport, M. M. Division of Neuroscience, N.Y. State Psychiatric Institute, New York, NY **Mechanism of interaction of myelin basic protein and S-100 protein: metal binding and fluorescence studies.** *Journal of Neurochemistry (Oxford)*. 27(1):173-177, 1976.

Studies of the binding of Ca²⁺ and Mn²⁺ to myelin basic protein and to S-100 protein and the alterations in conformation that take place in the presence of these ions are reported. Alterations in conformation are detected from changes in fluorescence. Both proteins exhibit this fluorescence which is attributable to the one tryptophan residue per mol that each contains. The myelin basic protein was isolated from bovine brain. The alteration of electrophoretic migration in gels of S-100 protein produced by Ca²⁺ and of MBP produced by Mn²⁺ are in accord with the observations based on fluorescence. Mn²⁺ does not affect the electrophoretic mobility of S-100. These results indicate that the formation of the complex between MBP and S-100 protein in the presence of either Ca²⁺ or Mn²⁺ is due to the conformational change induced by these ions in S-100 protein, MBP, or both. 10 references. (Author abstract modified)

001329 Phillips, M. E.; Coxon, R. V. University Laboratory of Physiology, Parks Road, Oxford OX1 3PT, England **Effect of insulin and phenobarbital on uptake of 2-deoxyglucose by brain slices and hemidiaphragms.** *Journal of Neurochemistry (Oxford)*. 27(2):643-645, 1976.

The effect of insulin and phenobarbital on uptake of 2-deoxyglucose by brain slices and hemidiaphragms has been investigated in vitro on cortical slices to avoid complications due to the blood-brain barrier or to hormones from other parts of the body acting on the brain. Experimental animals selected were rats, using hemidiaphragms from the same animals as a standard of reference in the experiments with insulin and as a representative nonnervous tissue with phenobarbital. It is demonstrated that the raffinose space of both tissues studied was unaffected by either insulin or phenobarbital. Insulin led to a small but significant increase in uptake of 2-deoxyglucose into brain slices, but its effect in increasing uptake into hemidiaphragm was marked. In contrast, phenobarbital caused a significant increase in uptake of 2-deoxyglucose by the brain but was without effect on the hemidiaphragms. It is concluded that phenobarbital exerts a direct and specific augmenting effect on the uptake of 2-deoxyglucose and presumably also of glucose itself by brain cells, with implications for hypoxia in experimental animals using anesthetic agents. 17 references.

001330 Phillis, J. W. Department of Physiology, College of Medicine, University of Saskatchewan, Saskatoon S7N 0W0, Saskatchewan, Canada **Is beta-(4-chlorophenyl)-GABA a specific antagonist of substance P on cerebral cortical neurons?** *Experientia (Basel)*. 32(5):593-594, 1976.

The specificity of beta-(4-chlorophenyl)-gamma-aminobutyric acid (beta-CPG) antagonism of substance P has been evaluated on neurons in the rat cerebral cortex, utilizing acetylcholine and L-glutamate induced excitations for comparisons. Beta-CPG antagonized the excitant actions of acetylcholine and substance P to comparable extents. L-glutamate induced excitation was affected to a lesser extent. These findings do not support the suggestion that beta-CPG is a specific substance P antagonist. 10 references. (Author abstract modified)

001331 Placidi, G. F.; Tognoni, G.; Pacifici, G. M.; Cassano, G. B.; Morselli, P. L. *Clinica Psichiatrica*, University of Pisa, Pisa, Italy **Regional distribution of diazepam and its metabolites in the brain of cat after chronic treatment.** *Psychopharmacology* (Berlin). 48(2):133-137, 1976.

A study was carried out in cats to determine the regional distribution of diazepam and its metabolites in the brain after administration of three doses daily for 5 days. Repeated administration of diazepam leads to remarkable accumulation of N-desmethyldiazepam in white matter structures and in subcortical areas such as thalamus, hypothalamus, and hypophysis. Diazepam and the hydroxylated metabolites were present in lesser amounts. The distribution pattern of diazepam and N-desmethyldiazepam offers a rationale for its efficacy in inhibiting spreading of seizures and for the lack of effect on primary foci discharges. The relevance of these findings to other factors pertaining to chronic treatment with diazepam is discussed. 22 references. (Author abstract modified)

001332 Polc, P.; Haefely, W. *Pharmaceutical Research Division, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland* **Effects of two benzodiazepines, phenobarbitone, and baclofen on synaptic transmission in the cat cuneate nucleus.** *Naunyn-Schmiedeberg's Archives of Pharmacology* (Berlin). 294(2):121-131, 1976.

The effects of diazepam, flunitrazepam, phenobarbital and baclofen on excitatory processes, presynaptic inhibitory processes and postsynaptic inhibitory processes in the cuneate nucleus were studied in decerebrate cats. Afferent presynaptic inhibition in the cuneate nucleus was markedly enhanced by diazepam and flunitrazepam, slightly enhanced by low doses of phenobarbital, and depressed by baclofen. Diazepam, flunitrazepam and phenobarbital also increased postsynaptic inhibition in the cuneate nucleus. Picrotoxin antagonized the effects of diazepam on presynaptic inhibition and postsynaptic inhibition. Thiosemicarbazide (TSC) nearly abolished the augmenting effect of diazepam on both types of inhibition. Phenobarbital, in contrast to the benzodiazepines, depressed the N wave in a dose dependent manner. Baclofen strongly depressed the cuneate N wave, decreased the excitability of CTR cells and reduced both presynaptic and postsynaptic inhibition, but had no effect on the resting excitability of primary afferent endings. It is suggested that: 1) benzodiazepines selectively enhance the GABA mediated presynaptic inhibition and postsynaptic inhibition in the cuneate nucleus; 2) phenobarbital slightly enhances inhibition only in a narrow dose range and reduces the excitatory processes in the cuneate nucleus; 3) baclofen depresses the excitation of cuneate relay cells and interneurons postsynaptically; and 4) the depression of relay cells by baclofen is probably nonspecific. 29 references. (Author abstract modified).

001333 Post, Robert M.; Kopanda, Richard T.; Black, Katherine E. *Section on Psychobiology, Adult Psychiatry Branch, NIMH, Bethesda, MD* **Progressive effects of cocaine on behavior and central amine metabolism in rhesus monkeys: relationship to kindling and psychosis.** *Biological Psychiatry*. 11(4):403-419, 1976.

Chronic biochemical effects of cocaine administration in the rhesus monkey were studied to shed light on the ethical questions that arise in the course of chronic stimulant administration in human volunteers to study euphoric and dysphoric mood disorders. A total of 13 rhesus monkeys received cocaine for up to 6 months in doses calculated to produce substantial behavioral effects. A subset of 7 monkeys received gradually increased doses to the level necessary to produce

convulsions. All monkeys were allowed drug free recovery periods of 2 days per week. Results reveal that chronic administration of the same dose of cocaine was associated with progressive alterations in pathological behavior and increased susceptibility to seizures. Monkeys initially displaying prominent hyperactive stereotypic responses for up to 2 months began to demonstrate increasing amounts of inhibitory behavior, consisting of catalepsy, motor inhibition, and abnormal visual tracking and staring. Four of thirteen animals developed increasing intensities of lingual/buccal dyskinesias after 10 weeks of chronic cocaine. Animals initially showing no convulsions to a given dose of cocaine eventually developed convulsions to the same dose, and then displayed an increased frequency of convulsions following subsequent injections. Levels of the dopamine metabolite, homovanillic acid (HVA), in the cisternal cerebrospinal fluid were significantly elevated during both excitatory stereotypic and inhibitory syndromes, and a similar trend was observed for HVA after probenecid administration. Only the probenecid/induced accumulations of the serotonin metabolite 5-hydroxyindoleacetic acid, following acute cocaine administration, were significantly elevated. The progressive increases in convulsions, dyskinesias, and the inhibitory syndrome did not appear related to alterations in peak levels of cocaine in plasma or cerebrospinal fluid, and a pharmacological kindling model is suggested as an alternate explanation of the data. It is concluded that results extend current models of stimulant induced psychoses by highlighting the progressive alterations in behavior and neurological sequelae and in suggesting that this progressive mechanism may also be important in the development of psychosis in man. 50 references. (Author abstract modified)

001334 Price, M. T. C.; Fibiger, H. C. *Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, B.C. V6T 1W5, Canada* **Abolition of nomifensine-induced stereotypy after 6-hydroxydopamine lesions of ascending dopaminergic projections.** *Pharmacology Biochemistry and Behavior*. 5(2):107-109, 1976.

The effects of bilateral focal injections of 6-hydroxydopamine (6-OHDA) into the zona compacta of the substantia nigra (SNc) on nomifensine induced stereotypy were examined in the rat. These lesions reduced neostriatal dopamine levels to less than 1% of control levels. They also abolished nomifensine induced stereotyped behavior. It is suggested that nomifensine induced stereotypy is mediated via a presynaptic action on dopamine uptake and release. 15 references. (Author abstract)

001335 Pugsley, T. A.; Merker, J.; Lippmann, W. *Department of Biochemical Pharmacology, Ayerst Research Laboratories, Montreal, Quebec, Canada H3C 3J1* **Effect of structural analogs of butaclamol (a new antipsychotic drug) on striatal homovanillic acid and adenylyl cyclase of olfactory tubercle in rats.** *Canadian Journal of Physiology and Pharmacology* (Ottawa). 54(4):510-515, 1976.

The effects of structural analogs of butaclamol on striatal homovanillic acid (HVA) and adenylyl cyclase of olfactory tubercle in rats were examined. The 3-isopropyl (I), 3-cyclohexyl (II), and 3-phenyl (III) analogs of butaclamol and their respective (d)-enantiomers caused a dose dependent elevation of rat striatal HVA concentration. This effect was indicative of an increased dopamine (DA) turnover; droperidol also exhibited this activity. The order of activity of the (d)-enantiomer in decreasing effectiveness was: II, I, III. A decrease in striatal DA was observed with (d)-I and (d)-III at the highest dose used, but not at 50% of the dose. Each analog antagonized the

DA induced increase in adenylyl cyclase activity of olfactory tubercle homogenates. The (d)-enantiomers of butaclamol analogs were two to four times more potent than their respective racemates, with (d)-butaclamol and (d)-I displaying activity generally equivalent to fluphenazine. The respective (l)-enantiomers were ineffective, indicating a stereochemical specificity for the DA receptor blockade. It is concluded that some analogs of this new antipsychotic agent should be effective in elucidating dopaminergic mechanisms. 31 references. (Author abstract modified)

001336 Puri, Surendra K.; Volicer, L.; Cochin, J. Dept. of Pharmacology and Experimental Therapeutics, Boston University School of Medicine, 80 East Concord St., Boston, MA 02118 **Changes in the striatal adenylyl cyclase activity following acute and chronic morphine treatment and during withdrawal.** *Journal of Neurochemistry (Oxford)*. 27(6):1551-1554, 1976.

The effects of acute and chronic morphine administration on dopamine sensitive adenylyl cyclase activity in the rat striatum after treatment and during withdrawal were investigated. Results show that acute i.p. administration of morphine caused a dose dependent increase striatal adenylyl cyclase activity, but did not affect dopamine stimulation of enzyme activity. Compared to nondependent controls, morphine dependent rats evidenced a two fold increase in the basal activity of adenylyl cyclase following chronic administration. Enzyme activity remained elevated up to 72 hours after the last morphine injection, but returned toward control level by 96 hours posttreatment. Adenylyl cyclase sensitivity to dopamine was significantly reduced in morphine dependent and morphine withdrawn rats. It is concluded that the characteristics of dopamine receptor molecules are modified by chronic, but not acute, morphine administration, and that morphine may activate dopamine receptors in the same way that dopamine does. 30 references.

001337 Pylatuk, K. L.; McNeill, J. H. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **The effects of certain drugs on the uptake and release of (3H)noradrenaline in rat whole brain homogenates.** *Canadian Journal of Physiology and Pharmacology (Ottawa)*. 54(4):457-468, 1976.

Twelve drugs were studied with respect to their effects on inhibition of neuronal uptake of 3H-noradrenaline (3H-NA) and on release of this amine from presynaptic nerve terminals. An in vitro method, using a crude synaptosomal homogenate prepared from rat whole brain, was employed. The 12 drugs were: tyramine, amitriptyline, nortriptyline, promethazine, desipramine, imipramine, phenindamine, triprolidine, chlorpheniramine, diphenhydramine, tripeleminamine, and cocaine. All drugs tested were found to produce some release of 3H-NA although tyramine was by far the most potent drug in this respect; tripeleminamine and cocaine were observed to produce the least release. Studies of inhibition of NA uptake again demonstrated tyramine to be the most potent of the 12 drugs produced uptake although in this case it did not differ significantly from cocaine and tripeleminamine. The remaining compounds also showed decreased accumulation of 3H-NA and all 12 drugs inhibition at a lower dose than that required for release of the amine. A correlation between releasing potency and lipophilicity of the compounds indicated that tyramine seemed to be acting in a different manner from the remaining compounds. A correlation between inhibitory potency and lipophilicity could be demonstrated for only six of the drugs, with tyramine, tripeleminamine and cocaine showing the

greatest deviation from this relationship. 29 references. (Author abstract)

001338 Ransom, Bruce R.; Barker, Jeffery L. Behavioral Biology Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20014 **Pentobarbital selectively enhances GABA-mediated postsynaptic inhibition in tissue cultured mouse spinal neurons.** *Brain Research (Amsterdam)*. 114(3):530-535, 1976.

Mouse spinal neurons grown in tissue culture were used to extend observations on pentobarbital's interactions with the putative inhibitory transmitters glycine and gamma-aminobutyric acid (GABA). It was found that pentobarbital acts selectively, by postsynaptic mechanisms, to prolong GABA-evoked conductance increase, while shortening or leaving unaltered the conductance increase to glycine. Part of this effect appears to be due to accentuation of a second, late component of the GABA response which has a different ionic mechanism. The actions of glycine and GABA on neuronal membrane conductance were quantitatively assessed, and it was demonstrated that glycine's duration of effect was shorter than GABA's when comparable applications were compared. The results help to explain the enhancing actions of pentobarbital on GABA mediated synaptic events and the variability of this drug's action on inhibitory pathways utilizing other transmitters such as glycine. 30 references.

001339 Razdan, Raj K.; Dalzell, Haldean C.; Herlihy, Patricia; Howes, John F. SISA Incorporated, Cambridge, MA 02138 **Unsaturated side-chain analogues of delta8-tetrahydrocannabinol with potent biological activity.** *Journal of Medicinal Chemistry*. 19(11):1328-1330, 1976.

Two delta8-THC derivatives, 4a and 4b, with functionalized side chains were synthesized. Treatment of (+)-trans-pmentha-2,8-dien-1-ol with the resorcinol 2b followed by removal of the dithiol group with HgO-BF₃·Et₂O gave the aldehyde 3b. A Wittig reaction of dimethyl (2-oxoheptyl) phosphate with 3b furnished 4a, which was reduced to 4b. Compounds 4a and 4b showed potent cannabinoid like activity in mice. 8 references. (Author abstract)

001340 Reyes, Edward; Palmer, Gene C. Univ. of New Mexico School of Medicine, Albuquerque, NM 87131 **Biochemical localization of gamma-glutamyl transpeptidase within cellular elements of the rat cerebral cortex.** *Research Communications in Chemical Pathology and Pharmacology*. 14(4):759-762, 1976.

Neuronal, glial enriched, and capillary enriched fractions of rat cerebral cortex were studied to determine the specific cellular localization of gamma-glutamyl transpeptidase within the cellular elements of the rat cerebral cortex. The data show that gamma-glutamyl transpeptidase is present in cellular elements other than capillaries as previously indicated by histochemical evidence. The enzyme was found to be in the purified neuronal fraction as well as the glial enriched and capillary enriched fractions. The capillary fraction contained the highest specific activity for the substrate gamma-glutamyl-p-nitroanilide. However, the neuronal fraction additionally displayed a substantial amount of enzyme activity, only slightly less than the capillary fraction. Although the maximal velocities for the enzymes differed from the neuronal, glial enriched and capillary enriched fractions they all exhibited the same Michaelis constant for the substrate, gamma-glutamyl-p-nitroanilide. This finding implies that the same enzyme form of gamma-glutamyl transpeptidase was assayed in all three cellular fractions. 10 references. (Author abstract modified)

001341 Riffée, W. H.; Gerald, M. C. College of Pharmacy, University of Texas, Austin, TX 78712 Effects of amphetamine isomers and CNS catecholaminergic blockers on seizures in mice. *Neuropharmacology* (Oxford). 15(11):677-682, 1976.

The effects of (+)-amphetamine and (-)-amphetamine on intravenous pentylenetetrazol (PTZ) induced clonic seizure threshold were studied in CD-1 mice. The (+) isomer elicited a biphasic effect, increasing seizure threshold 5% to 21% at low doses and decreasing PTZ induced clonic seizure threshold 15% to 28% at high doses. The minus amphetamine isomer increased PTZ induced clonic seizure threshold 28% to 49% doses of 15 to 45mg/kg were without effect. Studies utilizing blockers of alpha and beta-noradrenergic receptors suggest that the biphasic effects of (+)-amphetamine may be dependent upon alpha and beta-noradrenergic activation, while the decrease in PTZ induced clonic seizure threshold possibly also involves the dopaminergic system. The increase in PTZ induced clonic seizure threshold by (-)-amphetamine is primarily mediated by the beta-noradrenergic system with alpha-noradrenergic and dopaminergic involvement also possible. These results show quantitative differences in the relative potency of the amphetamine isomers, and suggest that qualitative differences may exist as well. 15 references. (Author abstract)

001342 Risner, Marc E.; Jones, B. E. National Institute on Drug Abuse, Addiction Research Center, Lexington, KY 40511 Role of noradrenergic and dopaminergic processes in amphetamine self-administration. *Pharmacology Biochemistry and Behavior*. 5(4):477-482, 1976.

The roles of noradrenergic processes and dopaminergic processes in d-amphetamine self-administration were studied in dogs trained to intravenously self-administer a stable quantity of the drug per session. Animals given nocontingent infusions of amphetamine immediately prior to a session decreased self-administration so that the total drug intake remained constant. There were no changes in amphetamine self-administration following pretreatment with the noradrenergic agonist methoxamine or the noradrenergic antagonist phenoxybenzamine. Responding was not maintained when methoxamine was substituted for amphetamine. Pretreatment with the dopaminergic antagonist pimozide or chlorpromazine produced dose dependent increases in the number of self-administered amphetamine infusions. It is suggested that noradrenergic neurotransmission is not responsible for d-amphetamine self-administration but that an intact dopaminergic system appears to be important. 33 references. (Author abstract modified)

001343 Robertson, H. A. Psychiatric Research Unit, University Hospital, Saskatoon, Saskatchewan S7N 0W8, Canada Octopamine, dopamine and noradrenaline content of the brain of the locust, *Schistocerca gregaria*. *Experientia* (Basel). 32(5):552-554, 1976.

The octopamine, dopamine, and noradrenaline content of the brain of the locust, *Schistocerca gregaria* has been determined using sensitive radiochemical enzymatic assays. Octopamine and dopamine are present in high concentration but the noradrenaline content is only 1/25 that of octopamine. Both reserpine and fusaric acid (a dopamine-beta-hydroxylase inhibitor) produce a significant depletion of the octopamine stores. The role of octopamine in the insect central nervous system remains obscure. 27 references. (Author abstract modified)

001344 Ronai, Andras Z.; Szekely, Jozsef I.; Graf, Laszlo; Dunai-Kovacs, Zsuzsa; Bajusz, Sandor. Research Institute for Pharmaceutical Chemistry, P.O. Box 82, H-1325 Budapest,

Hungary Morphine-like analgesic effect of a pituitary hormone, beta-lipotropin. *Life Sciences* (Oxford). 19(5):733-738, 1976.

The analgesic effect of beta/lipotropin (beta-LPH) and its fragments administered intracerebroventricularly (ICV) to rats was studied. beta-LPH proved to be a specific, morphine like analgesic processing 2.2 times weaker analgesic potency than morphine, calculated on molar base. Tryptic digest of beta-LPH or smaller fragments of the hormone (LPH-(61-65)-peptide and LPH-(61-69)-peptide) were devoid of significant analgesic activity. The in vivo results appeared to be in contrast to those previously obtained in longitudinal muscle strip of guinea-pig ileum, in vitro. One possible explanation of the apparent contradiction is discussed. 27 references. (Author abstract modified)

001345 Ross, S. B. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertälje, Sweden Long-term effects of N-2-chloroethyl-N-ethyl-2-bromobenzylamine hydrochloride on noradrenergic neurones in the rat brain and heart. *British Journal of Pharmacology* (London). 58(4):521-527, 1976.

The mechanism by which N-2-chloroethyl-N-ethyl-2-bromobenzylamine hydrochloride (DSP-4) exerts its long-term effects on noradrenergic neurons was studied in the rat brain and heart. Intraperitoneally injected DSP-4 was found to: 1) decrease noradrenaline (NA) uptake in various brain regions except the striatum; 2) decrease uptake of NA in the rat heart atrium; 3) decrease NA concentration in both brain and heart; 4) decrease dopamine-beta hydroxylase (DBH) activity in both brain and heart with greater effect occurring in the cerebral cortex than in the hypothalamus; and 5) have no effect on 5-hydroxytryptamine (5-HT) uptake in various brain regions. The long-term effects of DSP-4 on NA uptake, NA concentration and DBH activity in the brain were antagonized by desipramine. It is suggested that DSP-4 attacks membranous NA uptake sites, forming a covalent bond which results in degeneration of the nerve terminals. 11 references.

001346 Roszkowski, Adolph P.; Schuler, Margery E.; Schultz, Ronald. Syntex Research, 3401 Hillview Ave., Palo Alto, CA 94304 Augmentation of pentylenetetrazol induced seizures by tricyclic antidepressants. *Materia Medica Polona* (Warszawa). 8(2):141-145, 1976.

The effects of tricyclic antidepressants, barbiturates, and minor tranquilizers on pentylenetetrazol induced seizures were studied in male albino mice administered one of the following drugs: imipramine, amitriptyline, phenobarbital, diphenylhydantoin, diazepam, and trimethadione. Results confirm previous results which indicated that antidepressants of the imipramine class inhibit maximal electroshock seizures and tonic extension due to pentylenetetrazol. Paradoxically, minimal pentylenetetrazol clonic seizures were augmented by these agents, yet neither minimal nor clonic electroshock seizures were augmented but were probably inhibited by imipramine. It is noted that data resemble observed clinical effects of the tricyclic antidepressants. 17 references. (Author abstract modified)

001347 Rothman, Taube P.; Ross, Leonard L.; Gershon, Michael D. Department of Anatomy, Columbia University College of Physicians and Surgeons, New York, NY 10032 Separately developing axonal uptake of 5-hydroxytryptamine and norepinephrine in the fetal ileum of the rabbit. *Brain Research* (Amsterdam). 115(3):437-456, 1976.

The fetal ileum of the rabbit was studied. The adult myenteric plexus accumulated tritium when incubated with tritiated 5-HT. However, in addition to labeled 5-HT, tritiated 5-hydroxyindoleacetic acid and, when monoamine oxidase (MAO) was inhibited, 5-HT-o-glucuronide were found in the tissue. Two uptake processes differing in affinity could be defined. Only the high affinity process was saturable. Fetal ileum took up tritiated 5-HT but glucuronidation did not occur when MAO was inhibited. The uptake of tritiated 5-HT by the fetal ileum was due to a single, saturable, temperature sensitive process inhibited by ouabain. It was identical to the high affinity uptake found in adult tissue. This specific high affinity uptake could be found as early as the 16th day of gestation, 5 to 8 days before uptake of NE being. Light and electron microscopic radioautography revealed that the uptake of 5-HT was primarily into axons and a characteristic structure called the expanded process, both in the myenteric plexus. Both contained dense cored vesicles. Axons were not labeled by tritiated NE until after 24 days and the expanded process was never labeled by tritiated NE. The data shown that uptake of 5-HT is a property of a distinct system of axons in the mammalian myenteric plexus which develops prior to adrenergic axons during ontogeny. 48 references. (Author abstract modified)

001348 Roufogalis, B. D.; Thornton, M.; Wade, D. N. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada **Specificity of the dopamine sensitive adenylate cyclase for antipsychotic antagonists.** *Life Sciences (Oxford)*. 19(6):927-934, 1976.

The specificity for antipsychotic agents of the dopamine receptor coupled to adenylate cyclase in the striatum of the rat brain was studied. Chlorpromazine, haloperidol, and clozapine are approximately equipotent in antagonizing dopamine sensitive adenylate cyclase activity in homogenates of rat brain striatum, in contrast to the differences in clinical antipsychotic potencies reported by others. The antagonism appeared to occur at a structurally specific dopamine site, as inhibition by a series of chlorpromazine analogues of similar hydrophobicity exhibited a structural specificity similar to that found for their neuroleptic and cataleptic activities. Sulpiride, a dopamine antagonist with antipsychotic activity, and metoclopramide, a structurally related central dopamine antagonist, failed to inhibit the dopamine sensitive adenylate cyclase. Pretreatment of rats with haloperidol did not induce a supersensitive response of the adenylate cyclase to stimulation by dopamine or apomorphine or inhibition by clozapine. It was concluded that the dopamine sensitive adenylate cyclase may not be the site of action of all antipsychotic agents. 45 references. (Author abstract modified)

001349 Ruszczewski, Piotr. Zespół Neurofizjologii Centrum Medycyny Doswiadczalnej i Klinicznej PAN, 3 Dworkowa, 00-784 Warsaw, Poland **The protective action of certain anaesthetics and tranquilizers against the effects of hyperbaric oxygen.** *Acta Physiologica Polonica (Warszawa)*. 27(5):435-447, 1976.

The protective effects of pentobarbitone, hydroxydione and diazepam against acute and chronic toxicity of high pressure oxygen (HPO) were studied in rats. During exposure to hyperbaric oxygen body temperature and ECG were measured. Long-term observations of animals after exposure to HPO were conducted. Pentobarbitone and hydroxydione reduced the manifestations of acute toxicity but increased those of chronic toxicity. Diazepam reduced the manifestations of acute toxicity and seemed to counteract those of chronic tox-

icity. Lowering of body temperature of the animals which occurred during exposure to HPO was probably connected with manifestations of chronic toxicity. Observation of the cardiorespiratory functions suggested a possible connection between their disturbances and onset of seizures and development of oxygen induced paralysis. 25 references. (Journal abstract)

001350 Saarnivaara, L.; Mannisto, P. T. Department of Pharmacology, University of Helsinki Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Effects of lithium and rubidium on antinociception and behaviour in mice: I. Studies on narcotic analgesics and antagonists.** *Archives Internationales de Pharmacodynamie et de Therapie (Ghent)*. 222(2):282-292, 1976.

The effects of acute and chronic lithium chloride (LiCl) and rubidium chloride (RbCl) treatments on the antinociception caused by morphine, pethidine, methadone, pentazocine, nalorphine or naloxone were studied in mice using the hot plate and phenylquinone writhing tests. In both tests morphine, pethidine and methadone caused significant antinociception whereas the antagonistic drugs were almost inactive. Especially in the acute experiments where LiCl and RbCl had some effects on the behavior of the mice treated with the analgesics, LiCl mostly impaired motor coordination and motor activity whereas RbCl was inactive or had opposite effects. LiCl enhanced the decrease in rectal temperature whereas RbCl was mostly inactive. In the acute experiments where LiCl had some effects on the behavior of the mice treated with the analgesics, LiCl impaired motor coordination and motor activity whereas RbCl was inactive or had the opposite effects. 24 references. (Author abstract modified)

001351 Sabelli, H. C.; Mosnaim, A. D.; Vazquez, A. J.; Giardina, W. J.; Borison, R. L.; Pedemonte, W. A. Dept. of Pharmacology, Chicago Medical School, Chicago, IL **Biochemical plasticity of synaptic transmission: a critical review of Dale's principle.** *Biological Psychiatry*. 11(4):481-524, 1976.

A series of biochemical, electrophysiological, and behavioral studies designed to test the outgrowth of Dale's hypothesis of specific synaptic transmission that states that mental disorders and psychoactive drugs exert their effects on behavior through activation or blockade of one or more specific transmitters is reviewed. Results suggest the alternative view that at each monoaminergic synapse the action of the transmitter is modulated by several metabolically related substances: amine analogs; deaminated products; and possibly also amino acid precursors. In support of this view, evidence for the presence, synthesis, metabolism and biological activity (at the cellular level, using microelectrode techniques) of amino acid, amines, deaminated compounds metabolically related to catecholamines and serotonin is presented. The biological activity of the deaminated metabolites of catecholamines and serotonin is illustrated by the effects of their microiontophoretic administration upon cortical units. Rabbit brain is shown to synthesize a series of pharmacologically active non-catecholic phenylethylamines as byproducts of catecholamine metabolism. An expanded Dale's principle is proposed on the basis of these and similar findings, which states that each neuron is specific insofar as it releases the same pool of chemical messengers at all of its endings and synthesizes the same types of receptors. The revised hypothesis, however, provides for the biochemical plasticity necessary to explain the documented concomitants of neural activity. 107 references. (Author abstract modified)

001352 Sable-Amplis, R.; Agid, R. Institut de Physiologie, Université Paul Sabatier, 2, rue François Magendie, F-31400 Toulouse, France **Beta-Blockade of morphine-induced hyperlactacidemia in rabbits.** *Experientia* (Basel). 32(5):609-611, 1976.

The mechanism responsible for hyperlactacidemia following morphine administration in animals was studied in rabbits, investigating prevention of lactate accumulation by pretreating animals with adrenergic blocking agents (phenolamine and propranolol). Phenolamine treatment did not modify the action of morphine, but morphine induced lactate accumulation was completely abolished by simultaneous propranolol treatment. It is suggested that abnormally high brain lactate concentration might be related to the state of anxiety found in drug addicts under withdrawal, as recent reports have demonstrated the effectiveness of propranolol in treating anxiety in man and heroin addiction withdrawal. Results of the investigation suggest that morphine induced hyperlactacidemia results largely from anaerobic muscle glycogenolysis which is mediated by beta-adrenergic receptors, without alpha-receptor involvement. 14 references. (Author abstract modified)

001353 Samorajski, T.; Rolsten, C. Neurobiology of Aging Section, Texas Research Institute of Mental Sciences, Houston, TX 77030 **Chlorpromazine and aging in the brain.** *Experimental Gerontology*. 11(5/6):141-147, 1976.

The effects of long-term chlorpromazine (CPZ) therapy on the aging process were studied in mice. CPZ treated animals lost weight during the first three months of treatment. After seven months of treatment, there were no differences between CPZ treated mice and controls in the amounts of total protein, RNA, or DNA in the cerebellum, serotonin (5-hydroxytryptamine, 5-HT) in the forebrain, and dopamine in the caudate nuclei. There was a significant decrease in norepinephrine in the forebrain as well as a dose dependent diminution of lipofuscin pigment in the neurons of the nucleus reticularis gigantocellularis in the CPZ treated mice. A higher mortality rate occurred in the mice receiving 10 mg/kg CPZ (the dose associated with the greatest reduction in lipofuscin pigment). It is concluded that further study of the possible role of CPZ and its metabolites in the aging process is warranted. 33 references.

001354 Samvelyan, V. M. no address **Antispasmodic effects of etpenal.** *Protivosudorozhnaya aktivnost' etpenala. Zhurnal Eksperimental'noy i Klinicheskoy Meditsiny* (Yerevan). 16(1):54-58, 1976.

A study was made of Etpenal (Diethylaminopropylidiphenylacetate), synthesized at the ITOX AN Arm. SSR and approved for clinical use, using EEG of the effect it had on the biopotentials of the cortex and the subcortex of cats and rabbits. It was found that Etpenal blocks cholinergic receptors of the brain and has little effect on desynchronization reactions connected with blockage of impulses in the reticular formations of the brain. There is a clear connection between preparations that are effective in treatment of Parkinsonism and their capacity to forestall nicotine spasms in rabbits. 8 references.

001355 Sastry, Bhagavatula Sree Rama; Sinclair, John Gordon. Division of Pharmacology and Toxicology, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **Tonic inhibitory influence of supraspinal monoaminergic system on recurrent inhibition of an extensor monosynaptic reflex.** *Brain Research* (Amsterdam). 117(1):69-76, 1976.

The effects of various drugs which alter biogenic amine synaptic activity on inhibitions of the spinal monosynaptic reflex (MSR) were examined in cats. Recurrent inhibition of the extensor (quadriceps) monosynaptic reflex (MSR) was antagonized by a 5-hydroxytryptamine (5-HT) precursor, 5-hydroxytryptophan (5-HTP), and a specific 5-HT neuronal uptake blocker, fluoxetine, in unanesthetized decerebrate cats. This inhibition of the flexor MSR was not altered by fluoxetine. Cyproheptadine partially reversed the blocking actions of 5-HTP and fluoxetine and a thoracic cold block, which eliminates supraspinal inputs to the caudal spinal cord, also eliminated the blockade by fluoxetine on recurrent inhibition. Cyproheptadine or phenoxybenzamine, administered alone, enhanced recurrent inhibition of the extensor but not of the flexor MSR. Since a cold block increased recurrent inhibition of the extensor reflex in control animals but failed to alter the inhibition in animals pretreated with either DL/p-chlorophenylalanine or DL/alpha-methyl-p-tyrosine methyl ester, the monoaminergic system would appear to be tonically active. In addition the neuronal uptake blocker, imipramine, was more potent in antagonizing recurrent inhibition when injected intraarterially to the spinal cord than when administered intraarterially to the brainstem or intravenously, indicating that this agent acts in the spinal cord to block the inhibition. These results support the proposal that a supraspinal system involving 5-HT and noradrenaline antagonizes recurrent inhibition of the quadriceps MSR. This monoaminergic system is tonically active with the 5-HT nerve terminals located in the spinal cord. 25 references. (Author abstract)

001356 Sato, Mitsumoto. Dept. of Neuropsychiatry, Okayama University Medical School, Okayama, Japan **A study on psychomotor epilepsy with "kindled" cat preparations.** *Folia Psychiatrica et Neurologica Japonica* (Tokyo). 30(3):425-434, 1976.

The role of amygdala, hippocampus and septal area in psychomotor epilepsy, and a biochemical aspect of the kindled neurocircuits were examined by behavioral and electrographic methods. Hippocampal seizure developed into motor seizures after establishing secondary epileptogenesis in amygdaloid and globus pallidus. A secondary epileptogenesis in the hippocampus was not necessary for amygdaloid seizures to develop into generalized convulsions. The septal seizure development was almost identical to the hippocampal seizure development, suggesting that psychomotor epilepsy may not only be triggered by the hippocampal and amygdaloid focus but also by the septum and its related structures. In another experiment, the effects of various neuroactive agents on interictal discharge frequency was studied in amygdaloid and hippocampal kindled cats. Clear antagonistic action of L-dopa against reserpine or alpha-MPT induced increase of interictal spike discharge frequency was observed. Viewed in conjunction with a previous assay study of catecholamine that showed a marked depletion of both norepinephrine and dopamine in hippocampal kindled cat brain, it may be concluded that catecholamine inhibits the establishment and activation of the kindled epileptic neurocircuits. 14 references. (Journal abstract modified)

001357 Satoh, M.; Zieglansberger, W.; Herz, A. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan **Actions of opiates upon single unit activity in the cortex of naive and tolerant rats.** *Brain Research* (Amsterdam). 115(1):99-110, 1976.

The effects of microelectrophoretically applied and systemically administered opiates on neuronal discharge activity in the sensorimotor cortex of naive rats and morphine

tolerant/dependent rats were studied. In naive rats, low doses of phoretically applied morphine depressed spontaneous discharge activity but higher doses and repeated application frequently converted this effect into excitation. Naloxone antagonized only the depressant effect. Levorphanol mimicked the action of morphine; dextrorphan was inactive. Morphine depressed the excitatory action of L-glutamate and of acetylcholine by a naloxone antagonizable mechanism. Systemic administration of Fentanyl mimicked the inhibitory effect of morphine, an effect which was antagonized by naloxone. In chronically morphinized rats, the depressant effect of microelectrophoretically administered morphine was almost lacking; a naloxone resistant excitation was the predominant effect. The excitant effect of naloxone was increased and the effects of morphine on glutamate and acetylcholine were abolished. It is suggested that a postsynaptically located stereospecific receptor exists which mediates the inhibitory effects of opiates and which may be involved in the development of acute and chronic tolerance to these drugs. 27 references. (Author abstract modified)

001358 Sawa, Aiko; Oka, Tetsuo. Department of Pharmacology, School of Medicine, Tokai University, Isehara, Kanagawa 259-11, Japan **Effects of narcotic analgesics on serotonin metabolism in brain of rats and mice.** Japanese Journal of Pharmacology (Kyoto). 26(5):599-605, 1976.

The effects of narcotic analgesics on the brain 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) levels of rats and mice were investigated. The results suggest that morphine accelerates the release of brain 5-HT both in rats and mice, and that neither methadone nor pethidine alters the brain 5-HT and 5-HIAA levels in rats. The morphine induced increase in brain 5-HT turnover is likely to be involved in the morphine induced decrease in locomotor activity and hypothermia in rats. The activity decreasing effects of methadone or pethidine, on the other hand, are mediated by mechanisms different from those which mediate the effects of morphine. In contrast, an increase in brain 5-HT turnover in mice apparently does not play an important role on activity increasing effects of morphine but rather participates in other pharmacological effects of morphine. 27 references. (Author abstract)

001359 Sayers, Anthony C.; Burki, Hans R.; Ruch, Walter; Asper, Helmut. Research Institute Wander, Sandoz Research Unit, Wander Ltd., PO Box 2747, Bern, Switzerland **Anticholinergic properties of antipsychotic drugs and their relation to extrapyramidal side-effects.** Psychopharmacology (Berlin). 51(1):15-22, 1976.

The hypothesis that the anticholinergic properties of clozapine may obscure its effects as a dopamine antagonist was tested in rats. The effects of haloperidol, alone and in combination with atropine, were compared with those of clozapine, alone and in combination with physostigmine, in a variety of tests commonly used to characterize neuroleptic compounds. Clozapine in combination with physostigmine did not present the profile of activity of a classical neuroleptic agent. Haloperidol in combination with atropine did not present the same profile of activity as clozapine. Some effects of haloperidol, such as catalepsy, were antagonized by atropine, while others, such as induction of striatal DA receptor hypersensitivity, were enhanced. It is concluded that the interaction between dopaminergic and cholinergic systems in the striatum is highly complex, and that a neuroleptic possessing both potent DA receptor blocking activity and muscarinic anticholinergic activity, while being less likely to

cause Parkinsonism in patients, would be more likely to induce tardive dyskinesias. 25 references. (Author abstract modified)

001360 Schallek, W.; Johnson, T. C. Department of Pharmacology, Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Spectral density analysis of the effects of barbiturates and benzodiazepines on the electrocorticogram of the squirrel monkey.** Archives internationales de Pharmacodynamie et de Therapie (Ghent). 223(2):301-310, 1976.

To compare the effects of benzodiazepines and barbiturates on gross behavior and on the electrocorticogram (ECOG), pentobarbital and diazepam were compared in a series of tests in squirrel monkeys, and phenobarbital and flurazepam were compared in a second series. The two barbiturates induced sedation, which was occasionally so deep that the monkeys could not be readily aroused. The benzodiazepines induced sedation in some monkeys, but others showed signs of restlessness. The ECOG showed general slowing with the barbiturates, whereas the benzodiazepines produced mixed fast and slow patterns. Spectral density analysis showed that pentobarbital increased activity at frequencies below 40 Hz, with the largest increases occurring below 8Hz. Phenobarbital increased activity below 8Hz, but differed from pentobarbital by decreasing activity above 13Hz. The benzodiazepines increased activity below 8Hz, decreased it between 8 and 20Hz, and increased it between 20 and 50Hz. 9 references. (Author abstract modified)

001361 Schneider, D.; Swamy, V. C. Dept. of Biochemical Pharmacology, School of Pharmacy, State Univ. of New York at Buffalo, Buffalo, NY 14214 **Persistent enhancement of potassium-induced responses of the rat vas deferens by desipramine.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 293(2):191-193, 1976.

The effect of desipramine on the cumulative dose response curves of noradrenaline and potassium was examined on the isolated rat vas deferens. An exposure of 10 to the minus 7th power M desipramine caused leftward shift and an increase in the maximum response of cumulative dose response curves of noradrenaline. Desipramine (10 to the minus 7th power M), in contact with the tissue for 10 min, enhanced responses to cumulative additions of potassium without causing a consistent change in threshold concentrations. Washout of desipramine resulted in a rapid loss of enhanced maximum response to noradrenaline while the maximum response to potassium did not show any decrease for up to 120 min after washout of drug. One possible explanation for the persistent enhancement of potassium induced response may be that desipramine causes postjunctional changes which selectively influence contractile responses of this tissue to potassium. 13 references. (Author abstract)

001362 Sedvall, Goran; Uvnas, Borje; Zotterman, Yngve. no address **Antipsychotic drugs: pharmacodynamics and pharmacokinetics.** Wenner-Gren Center International Symposium Series, Volume 25. New York, Pergamon Press, 1976. 468 p. \$35.00.

Papers presented at a symposium on the mechanisms of action, pharmacokinetics and clinical use of antipsychotic drugs are published in this volume. There are a number of chapters on animal model experiments. The majority of the book is concerned with biochemical pharmacology, including structure/activity relationships and theories concerning the extrapyramidal effects of various compounds. Several papers deal the presynaptic and postsynaptic dopamine receptors, excitatory effects vs inhibitory effects at dopamine receptors,

and dopamine sensitive adenylate cyclase. Several papers describing clinical studies are also included.

001363 Seeber, U.; Kuschinsky, K. Department of Biochemical Pharmacology, Max Planck Institut für experimentelle Medizin, Hermann Rein Str, D-3400 Göttingen, Germany **Dopamine-sensitive adenylate cyclase in homogenates of rat striata during ethanol and barbiturate withdrawal.** Archives of Toxicology (Berlin). 35(4):247-253, 1976.

Repeated administrations of ethanol and of phenobarbital to rats led to characteristic withdrawal symptoms when the drug had been stopped. Since both drugs affect brain dopamine metabolism the postjunctional sensitivity to dopamine in the corpora striata was tested during ethanol or phenobarbital withdrawal. This was done by studying the dopamine sensitive adenylate cyclase in homogenates of the corpora striata of ethanol or phenobarbital dependent rats. The results demonstrated a slight postjunctional subsensitivity to dopamine in withdrawal from both ethanol and phenobarbital. Both drugs when added in vitro did not affect the postjunctional sensitivity to dopamine. The results do not support the hypothesis, at least not in the case of dopamine, that a postjunctional supersensitivity to neurotransmitters is important for withdrawal symptoms after chronic administration of drugs inducing physical dependence. 14 references. (Journal abstract)

001364 Sergeev, P. V.; Vedernikova, N. N.; Mayskiy, A. I. II Moskovskogo meditsinskogo instituta im. N. I. Pirogova, Moscow, USSR **Is the induction of microcosmal liver enzymes causative of tolerance to barbiturates?** Yavlyayetsya li induktsiya mikrosomnykh fermentov pecheni prichinoy tolerantnosti k barbituratom? Farmakologiya i Toksikologiya (Moskva). 39(2):208-212, 1976.

In experiments with female rats the enzyme induction action of single doses of phenobarbital, sodium barbital and sodium pentobarbital was shown to cause an increased synthesis of protein in the cellfree protein synthesizing system and a rise in the level of cytochromes b5 and P-450. In parallel chronic experiments the nature and time of the appearance of tolerance to these substances were determined. There is a lack of correlation between the power of the inductor and the speed with which tolerance develops, and therefore it is argued that induction is not the main cause of the development of tolerance to barbiturates. 13 references. (Author abstract modified)

001365 Sethy, Vimala H. 678 South Drake Road, Kalamazoo, MI 49009 **Effects of chronic treatment with neuroleptics on striatal acetylcholine concentration.** Journal of Neurochemistry (Oxford). 27(1):325-326, 1976.

The hypothesis that if neuroleptic induced Parkinsonism is related to excessive release of acetylcholine and reduction in its concentration in the striatum, then the disappearance of this effect may be associated with normalization of striatal acetylcholine concentration, is tested. The method of testing the hypothesis was to investigate the effect of chronic treatment with antipsychotic drugs on striatal acetylcholine concentration. The implications of the results are discussed in terms of several theories that are proposed to explain the mechanism of action. 16 references.

001366 Sewell, R. D. E.; Spencer, P. S. J. Applied Pharmacology Laboratories, Welsh School of Pharmacy, UWIST, Cardiff, Wales **Antinociceptive activity of narcotic agonist and partial agonist analgesics and other agents in the tail-immersion test in mice and rats.** Neuropharmacology (Oxford). 15(11):683-688, 1976.

The antinociceptive activity of a series of narcotic agonist (morphine like) and partial agonist (pentazocine like) agents was assessed in both mice and rats using a tail immersion nociceptive test. Narcotic agonist agents (diamorphine, etorphine, morphine, and pethidine) displayed characteristically steep and parallel log dose response lines in both species, whether administered peripherally or centrally. The partial agonists examined (cyclazocine, nalorphine, and pentazocine) also produced parallel but much shallower log dose response lines of essentially different slope to the agonists. The claimed pure antagonist naloxone also exhibited low order antinociceptive activity, with a dose response line parallel to that of the partial agonists. The tail immersion test in mice showed specific sensitivity to narcotic agonists and partial agonists, while peripherally acting analgesics (e.g., aspirin, indomethacin, paracetamol, and sodium salicylate) were generally inactive. It is therefore suggested that this test would be of particular value in assessing antinociceptive activity of the partial agonist type in small laboratory animals. 33 references. (Author abstract)

001367 Seyfried, C.; Nowak, H.; Wolf, H. P. Medizinische Forschung, E. Merck, D-6100 Darmstadt, Germany **The influence of mepiprazol on monoamine metabolism in the CNS of the rat: demonstration of diminished norepinephrine activity under simultaneously increased serotonin and dopamine activity.** Der Einfluss von Mepiprazol auf den Monoaminstoffwechsel im ZNS der Ratte: Nachweis verminderter Noradrenalin-Aktivität unter gleichzeitig erhöhter Serotonin- und Dopamin-Aktivität. Arzneimittelforschung (Aulendorf). 26(6):1088-1090, 1976.

The effect of mepiprazol, a new psychotropic agent, on the metabolism of biogenic amines was studied in the rat brain. Male Wistar rats weighing 150 to 200g were used. Brain norepinephrine, dopamine, and serotonin were determined fluorometrically. Mepiprazol, 1.25mg/kg, strongly enhanced the decrease in norepinephrine concentration brought about by alpha-methyltyrosine, but the decrease in dopamine concentration was unaffected. In contrast, mepiprazol partially reversed the decrease in serotonin concentration brought about by alpha-propyldopacetamide. Mepiprazol inhibited the release of serotonin precipitated by 4-methyl-alpha-ethyl-m-tyramine, and the release dopamine produced by 4, alpha-dimethyl-m-tyramine, but had no effect on the release of norepinephrine induced by 4, alpha-dimethyl-m-tyramine. It is concluded that mepiprazine may be helpful in certain types of depression, and in alleviating side-effects of L-dopa in the treatment of parkinsonism. 23 references.

001368 Shapiro, B. H.; Goldman, A. S.; Steinbeck, H. F.; Neumann, F. Division of Experimental Pathology, Children's Hospital of Philadelphia, Philadelphia, PA 19104 **Is feminine differentiation of the brain hormonally determined?** Experientia (Basel). 32(5):650-651, 1976.

From observation that gonadotropin secretion in the pseudohermaphrodite rat is not cyclic (indicating that in the absence of androgen imprinting this parameter of sexual differentiation does not result in expression of the female phenotype), a study was conducted to determine whether another aspect of neural differentiation (sexual behavior) is expressed as female in the pseudohermaphrodite. Pseudohermaphrodites and their normal King-X Holtzman littermate males and nonlittermate females were housed in temperature and humidity controlled animal quarters with illumination of 12 hours each of light and darkness and testing commenced at the beginning of the dark period. All rats were gonadectomized 1 month be-

fore behavioral testing. Before testing for feminine sexual behavior rats received estradiol benzoate and progesterone. Each rat was introduced into an observation cage with a male of proven sexual vigor and feminine sexual behavior was observed and rated as positive for feminine sexual response for repeated lordosis within a 10 minute test period. Before testing for masculine sexual behavior rats were injected with testosterone propionate. These animals were observed in behavior with normal spayed female rats, counting two mounts with pelvic thrusting within 5 minutes as indicative of male sexual behavior. Results showed that normal male and female rats treated with homotypical sex hormones displayed the usual dimorphic sexual behaviors. The pseudohermaphrodites exhibited no sexual response. Results suggest that feminine differentiation of the brain requires active imprinting by perinatal hormones, possibly adrenal progesterone. 22 references. (Author abstract modified)

001369 Sharma, Raghubir P. Toxicology Program and Department of Veterinary Science, Utah State University - 56, Logan, UT 84322 **Influence of dieldrin on serotonin turnover and 5-hydroxyindole acetic acid efflux in mouse brain.** *Life Sciences (Oxford)*. 19(4):537-541, 1976.

To examine the neurotoxic mechanism of organochlorine insecticides and their influence on serotonin turnover and 5-hydroxyindole acetic acid efflux, chronic doses of dieldrin were administered to mice. Such administrations failed to produce any alteration of brain serotonin, norepinephrine, or dopamine, but caused an increase in 5-hydroxyindole acetic acid levels. The turnover rate of serotonin was unaffected by dieldrin. The probenecid induced accumulation rate of 5-hydroxyindole acetic acid was considerably lowered in dieldrin treated mice. The results suggested a possible influence of dieldrin on 5-hydroxyindole acetic acid efflux from mouse brain. 17 references. (Author abstract modified)

001370 Shaw, J. P.; Ratcliffe, F. School of Pharmacy, Brighton Polytechnic, Brighton, England **Effect of lithium on brain 5-hydroxytryptamine metabolism in mice.** *Archives Internationales de Pharmacodynamie et de Therapie (Ghent)*. 222(1):116-124, 1976.

The effect of lithium carbonate on brain 5-hydroxytryptamine (5-HT) metabolism was studied in mice by determining the effects of lithium on brain 5-HT levels, brain monoamine oxidase (MAO) activity and 5-hydroxytryptophan decarboxylase activity, 5-HT accumulation after treatment with pargyline, 5-HT depletion after treatment with parachlorophenylalanine (PCPA) and 5-hydroxyindoleacetic acid (5-HIAA) accumulation after probenecid. An increase in the synthesis and breakdown of brain 5-HT occurs in the presence of lithium with no change in brain 5-HT levels. It is concluded that the increased turnover of 5-HT in the presence of lithium is due to an increased release, reuptake, and intraneuronal breakdown of 5-HT. 23 references.

001371 Sheard, Michael H.; Davis, Michael. Yale University School of Medicine, 34 Park Street, New Haven, CT 06508 **p-Chloroamphetamine: short and long term effects upon shock-elicited aggression.** *European Journal of Pharmacology (Amsterdam)*. 40(2):295-302, 1976.

The effects of para-chloroamphetamine (PCA) on shock elicited aggression were investigated in rats. PCA inhibited shock elicited aggression 15 min after administration but facilitated fighting 2 h after administration. The latter effect persisted for 4 weeks. Both the inhibitory effects and the excitatory effects of PCA were dose related and were blocked

by pretreatment with parachlorophenylalanine (which significantly reduces serotonin (5-HT) levels in the brain) but not by alpha-methyl-para-tyrosine (which significantly reduces the levels of other brain catecholamines). PCA increased pain thresholds 15 min after injection and then decreased pain thresholds for the next 24 h. The results are consistent with the hypothesis that inhibition of shock elicited aggression is associated with enhanced release of 5-HT whereas enhancement of shock elicited aggression is associated with 5-HT depletion. 26 references. (Author abstract modified)

001372 Shimazu, Takashi; Matsushita, Hiroshi; Ishikawa, Koichi. Div. of Neurochemistry, Psychiatric Research Institute of Tokyo, Kamikitazawa, Setagaya, Tokyo, Japan **Cholinergic stimulation of the rat hypothalamus: effects on liver glycogen synthesis.** *Science*. 194(4264):535-536, 1976.

To gain further insight into the regulatory function of the lateral hypothalamic nucleus in liver metabolism, neurons of the rat lateral hypothalamus were selectively stimulated with local applications of the different neurotransmitters, and changes in the activity of liver glycogen synthase, an enzyme catalyzing the rate limiting step in glycogen biosynthesis, were studied. Cholinergic stimulation of the lateral hypothalamic neurons with intrahypothalamic microinjections of acetylcholine or carbachol caused a marked increase in the content of the active form of glycogen (starch) synthase in the liver. Total activity of the enzyme (active plus inactive forms) was not increased significantly. Similar applications of other neurotransmitters, such as norepinephrine, dopamine, serotonin, and gamma-aminobutyric acid, did not affect the enzyme's activity. 7 references.

001373 Siemens, Albert J.; Chan, Arthur W. K. Research Institute on Alcoholism, 1021 Main Street, Buffalo, NY 14203 **Differential effects of pentobarbital and ethanol in mice.** *Life Sciences (Oxford)*. 19(4):581-589, 1976.

The differential sensitivity of long sleep (LS) and short sleep (SS) mice to ethanol was studied to determine if it is specific to this compound or whether it would occur with other hypnotics such as pentobarbital (PB). The duration of righting reflex (RR) loss after intraperitoneal injections of ethanol was significantly longer in LS than in SS mice and was correlated with differences in brain sensitivities to ethanol. Doses of PB produced a significantly longer loss of RR in SS than in LS mice. PB concentrations in the brain were the same in both mouse strains at the time of RR recovery, suggesting equal sensitivities of the central nervous systems to PB. The rates of disappearance of PB from the blood were the same in both strains, but the apparent volume of distribution of PB in the LS strain was greater than in SS mice. 15 references. (Author abstract modified)

001374 Silvestrini, B.; Lisciani, R. F. Angelini Research Institute, Viale Amelia 70, Rome, Italy **Experimental data suggesting an adrenergic mechanism in the production of Parkinsonian symptoms.** *Current Therapeutic Research*. 20(5):716-724, 1976.

The effects of atropine, pyrilamine, dibenzylamine, p-chlorophenylalanine, 5-hydroxytryptophan, imipramine, trazodone and etoperidone on tremor produced by oxotremorine and clonidine and nicotine were studied in mice. Their effects on oxotremorine induced salivation and clonidine induced piloerection were also recorded. Oxotremorine induced tremor was inhibited by atropine, dibenzylamine, imipramine, trazodone and etoperidone; the other drugs had no effect. Oxotremorine induced salivation was inhibited by atropine and

imipramine but was not affected by dibenzylamine, trazodone and etoperidone. Clonidine induced tremor and piloerection were inhibited by dibenzylamine, trazodone and etoperidone; atropine and imipramine potentiated the tremor, but had no effect on piloerection. The other drugs had no effect on either tremor or piloerection. Nicotine induced tremor was inhibited by trazodone and etoperidone; according to the literature, it is also inhibited by pyrilamine and dibenzylamine, whereas atropine has no effect. The only property common to dibenzylamine, trazodone and etoperidone, which inhibit all three types of tremor, is their adrenergic action. Thus, an adrenergic mechanism appears to represent a step of crucial importance for any type of tremor. This hypothesis is consistent with the clinical observations. 40 references. (Author abstract)

001375 Skolnick, Phil; Daly, John W. National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, MD 20014 **Interaction of clonidine with pre- and post-synaptic adrenergic receptors of rat brain: effects on cyclic AMP-generating systems.** *European Journal of Pharmacology (Amsterdam)*. 39(1):11-21, 1976.

The locus and mechanism of interaction of clonidine with catecholamine elicited accumulations of cyclic AMP has been investigated in brain slices from control and 6-hydroxydopamine (6-OHDA) treated rats. Clonidine inhibits the norepinephrine stimulated accumulation of cyclic AMP and potentiates the isoproterenol stimulated accumulation of cyclic AMP to the same extent in cerebral cortical slices from control and 6-OHDA treated rats. Clonidine has no intrinsic stimulatory activity on cortical cyclic AMP generating systems from either control or 6-OHDA treated rats. Phenoxybenzamine elicits a significant accumulation of C-AMP in cerebral cortical slices which can be abolished by pretreatment of rats with 6-OHDA or by incubation of tissue slices with either clonidine or sotalol. The hyperresponsiveness to catecholamines usually observed following central administration of 6-OHDA failed to develop. Concentrations of phenoxybenzamine which have no significant stimulatory effects on cyclic AMP accumulation can abolish the potentiative effects of clonidine on isoproterenol stimulated formation of cyclic AMP. The beta-antagonist, sotalol, is a less effective antagonist of isoproterenol stimulated accumulation of cyclic AMP in the presence of clonidine. Clonidine has no significant effect on the accumulation of cyclic AMP elicited by submaximal concentrations of isoproterenol in cerebellar slices. The data are consistent with the hypothesis that both the inhibitory effects on norepinephrine stimulated accumulation of cyclic AMP and the stimulatory effects of clonidine on isoproterenol elicited accumulation of cyclic AMP are exerted at postsynaptic alpha-adrenoceptors. No evidence was found for a presynaptic generation of cyclic AMP, although clonidine does reverse the stimulatory effects of phenoxybenzamine on cyclic AMP accumulation, presumably by interaction with a presynaptic site controlling norepinephrine release. 30 references. (Author abstract modified)

001376 Skolnick, Phil; Daly, John W. National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH, Bethesda, MD 20014 **Antagonism of alpha- and beta-adrenergic-mediated accumulations of cyclic AMP in rat cerebral cortical slices by the beta-antagonist (-)alprenolol.** *Life Sciences (Oxford)*. 19(4):497-503, 1976.

Antagonism of alpha-adrenergic and beta-adrenergic mediated accumulations of cyclic AMP in rat cerebral cortical slices by the beta-antagonist (-)alprenolol, a compound reported to bind with a high degree of specificity and

stereoselectivity to beta-adrenergic receptors from rat cerebral cortex, is reported. The (-)alprenolol completely inhibited the accumulations of cyclic AMP elicited by maximally effective concentrations of norepinephrine and epinephrine at antagonist concentrations as low as 10 to the minus 5M. Other beta-adrenergic antagonists such as (-)propranolol, (+)sotalol, and (+)alprenolol only partially antagonized accumulations of cyclic AMP elicited by these catecholamines even at 10 fold higher concentrations. Alpha-adrenergic antagonists such as phentolamine, phenoxybenzamine, and clonidine only partially antagonized the catecholamine response. (-)Alprenolol also completely inhibited the accumulation of cyclic AMP elicited by methoxamine, a compound shown to stimulate the accumulation of cyclic AMP by interaction with alpha-adrenergic receptors. The results indicate that in brain tissues containing a mixed population of alpha and beta adrenergic linked cyclic AMP generating systems, (-)alprenolol does not exhibit absolute specificity for beta-receptors. 27 references. (Author abstract)

001377 Slotkin, Theodore A.; Lau, Christopher; Bartolome, Maria; Seidler, Frederic J. Department of Physiology and Pharmacology, Duke University Medical Center, Durham, NC 27710 **Alteration by methadone of catecholamine uptake and release in isolated rat adrenomedullary storage vesicles.** *Life Sciences (Oxford)*. 19(4):483-491, 1976.

The mechanisms by which exposure of isolated adrenomedullary vesicles to methadone in vitro alters both uptake and release of catecholamines were examined and contrasted with those of morphine. Incubation of isolated rat adrenomedullary storage vesicles with methadone produced inhibition of 3H-epinephrine uptake and promotion of release of endogenous catecholamines. Neither effect was seen using morphine, nor could morphine antagonize methadone induced catecholamine release, suggesting that these actions are not mediated by opiate receptors. Inhibition of uptake by methadone appeared to contain a competitive component compared to 3H-epinephrine. Despite competitive inhibition by methadone, the maximal uptake capacity (analogous to Vmax) as determined by double reciprocal plots, was increased by the drug, probably as a result of greater availability of intravesicular storage sites because of the drug induced release of endogenous catecholamines. Agents which enhance or block catecholamine transport into vesicles had no effect on the catecholamine release by methadone, indicating that the latter is separable from the action on uptake. These alterations of catecholamine uptake and release may play a role in the effects of methadone on the adrenal medulla in vivo. 22 references. (Author abstract)

001378 Slotkin, Theodore A.; Lau, Christopher; Bartolome, Maria. Department of Physiology and Pharmacology, Duke University Medical Center, Durham, NC 27710 **Effects of neonatal or maternal methadone administration on ornithine decarboxylase activity in brain and heart of developing rats.** *Journal of Pharmacology and Experimental Therapeutics*. 199(1):141-148, 1976.

The effects of methadone on the developmental pattern of ornithine decarboxylase (ODC) activity and on organ weights were examined in heart and brain. To dissociate drug effects on the mother from those on the offspring, maternal drug administration has been contrasted with methadone administered directly to the pup, and, in addition, the effects of different periods of drug exposure and of neonatal withdrawal have been determined. The data show that exposure to methadone during fetal and/or neonatal life produces alterations in

polyamine metabolism which may result in abnormal organ development. The type of change is dependent upon the period and route of exposure and may reflect both direct effects on the pup and indirect effect from drug induced alterations in maternal metabolism or behavior. 33 references. (Author abstract modified)

001379 Smiley, Kathleen A.; Karler, Ralph; Turkanis, Stuart A. Dept. of Pharmacology, Univ. of Utah College of Medicine, Salt Lake City, UT 84132 **Effects of cannabinoids on the perfused rat heart.** Research Communications in Chemical Pathology and Pharmacology. 14(4):659-675, 1976.

The in vitro effects of delta9-tetrahydrocannabinol (delta9-THC), as well as those of three other naturally occurring cannabinoids, delta8-THC, cannabidiol (CBD) and cannabitol (CBN), on the rate and contractility of the isolated perfused rat heart were studied. All drugs depressed myocardial contractility. Their effect on rate, however, was not uniform: delta8-THC produced cardiac arrhythmias but no other consistent change; both delta9-THC and CBN caused tachycardia; but CBD produced bradycardia, arrhythmias, and asystole. In addition, as a consequence of the disposition of the cannabinoids to accumulate in the isolated heart, high tissue concentrations appeared in conjunction with the direct cardiac effects. 31 references. (Author abstract)

001380 Smith, Donald F. Psychopharmacology Research Unit, Psychiatric Hospital, 8240 Risskov, Denmark **Locomotor activity and plasma, red blood cell and cerebral cortex lithium concentration in inbred mice given lithium carbonate.** Pharmacology Biochemistry and Behavior. 5(4):379-382, 1976.

The effects of lithium carbonate on locomotor activity were studied in inbred male mice of the C57, BALB, C3H and DBA strains and the concentrations of lithium in the plasma, red blood cells and cerebral cortex were determined. The C3H mice were most susceptible to the activity suppressant effects of lithium, DBA mice were less susceptible to the drug, and the BALB and C57 mice were least susceptible. No relationship was found between the pharmacokinetics of lithium and its effects on activity. The findings are consistent with the notion that genetic factors can influence the effects of lithium on behavior, but they do not support the hypothesis that genetic determination of lithium uptake into cells is responsible for these effects. 24 references. (Author abstract modified)

001381 Snow, Anne E.; Horita, A. Department of Pharmacology, University of Washington School of Medicine, Seattle, WA 98195 **The stress-dependent nature of apomorphine hyperthermia.** Brain Research (Amsterdam). 117(1):163-168, 1976.

The stress dependent nature of hyperthermia produced by apomorphine in rabbits restrained in a stanchion was examined. The hyperthermia produced by apomorphine administration to restrained rabbits was reduced by releasing the rabbits from the stanchion. Similarly, when apomorphine was administered to unrestrained rabbits, the temperature increased less than 0 degrees Centigrade for all doses of the drug. Total body restraint produced results similar to those of unrestrained animals. When the animals were given amphetamine prior to the administration of apomorphine all the stanchion restrained animals exhibited hyperthermia while unrestrained animals were unaffected by the combined treatment. The role of restraint in sensory responsiveness is discussed in conjunction with the role of brain dopaminergic and noradrenergic systems in the mediation of these responses. 11 references.

001382 Spano, P. F.; Di Chiara, G.; Tonon, G. C.; Trabucchi, M. Dept. of Pharmacology and Pharmacognosy, University of Milan, Milan, Italy **A dopamine-stimulated adenylate cyclase in rat substantia nigra.** Journal of Neurochemistry (Oxford). 27(6):1565-1568, 1976.

To provide a highly specific model for studying dopamine receptor function in the substantia nigra, dopamine stimulated adenylate cyclase activity was measured in rat and calf substantia nigra. Preliminary findings of a dopamine effect on adenylate cyclase were tested by determining concentration/response curves for dopamine, 1-norepinephrine, and 1-isoproterenol in the rat brain. Results indicate that dopamine stimulated cyclic adenosine monophosphate (cAMP) formation over basal levels even in low concentrations, while 1-norepinephrine had no effect at low concentrations. The maximal stimulation of adenylate cyclase produced by 1-norepinephrine, however, was of the same order as that observed with dopamine. Higher concentrations of 1-norepinephrine were required to achieve maximal stimulation. The beta-adrenoceptor agonist 1-isoproterenol had no effect on adenylate cyclase of the substantia nigra. Apomorphine increased cAMP formation over basal levels. Haloperidol and fluphenazine completely blocked dopamine stimulated increases in adenylate cyclase activity. Implications of these findings are discussed. 25 references.

001383 Spano, P. F.; Kumakura, K.; Govoni, S.; Trabucchi, M. Department of Pharmacology and Pharmacognosy, University of Milan, Milan, Italy **Ontogenetic development of neostriatal dopamine receptors in the rat.** Journal of Neurochemistry (Oxford). 27(2):621-624, 1976.

The actions of dopamine and apomorphine on the kinetic properties of striatal adenylate cyclase were investigated during ontogenesis in the rat. The maximum stimulatory effect of dopamine was constant from birth to maturity (1 to 60 days of age). In contrast, the stimulatory effect elicited by apomorphine was almost the same as that of dopamine in 6-day-old rats, but it declined during maturation reaching 50% of the initial value at 60 days of age. The apparent kinetic activity value for dopamine did not change during development, while for apomorphine it was higher in the adult than in the newborn. Apomorphine appeared to have a greater affinity than dopamine for the striatal adenylate cyclase both in adult and newborn rats. Several hypotheses were derived from the data, relating ontogenetic changes in neostriatal dopamine receptors to the action of dopaminergic agonists and antagonists. 21 references. (Author abstract modified)

001384 Spencer, John; Revzin, Alvin. Behavioral Sciences Department, Naval Medical Research Institute, Bethesda, MD 20014 **Amphetamine, chlorpromazine and clonidine effects on self-stimulation in caudate or hypothalamus of the squirrel monkey.** Pharmacology Biochemistry and Behavior. 5(2):149-156, 1976.

The effects of different doses and duration of action of amphetamine, chlorpromazine, and clonidine on intracranial self-stimulation (ICSS) were investigated in the squirrel monkey. Low rates of ICSS elicited from the caudate or lateral hypothalamus are increased by low doses of amphetamine; thresholds for responding are decreased. Increasing the amphetamine dose inhibits responses at both brain sites. The inhibitory effect of amphetamine on ICSS from the medial forebrain bundle (MFB) area of the lateral hypothalamus is 6 hr. At caudate sites ICSS occurs only after 48 hr. Large doses of amphetamine increase the duration of action at both sites. Chlorpromazine (CPZ) decreases caudate ICSS significantly

more than lateral hypothalamic ICSS. The duration of action of small doses of CPZ is 6 hr at lateral hypothalamic brain sites and 24 hr at caudate sites. The duration of action of larger doses of CPZ is 12 hr in the MFB and 36 hr in the caudate. A low dose of clonidine blocks high rates of MFB ICSS and has much less effect on caudate ICSS. Higher doses of clonidine sedate the animals and inhibit ICSS equally at both sites. It is suggested that: 1) the effects of amphetamine and CPZ involve not only hypothalamic structures but more anterior telencephalic structures as well; 2) drugs acting in part on dopamine containing neurons will interfere with certain caudate mediated behavior; and 3) since hypothalamic but not caudate ICSS sites are more dose sensitive to drugs that selectively act on norepinephrine (NE) containing neurons, other amines in addition to NE may be involved in ICSS. 30 references. (Author abstract modified)

001385 Sprague, G.; Craigmill, A. College of Pharmacy, Washington State University, Pullman, WA 99163 **Behavioral and metabolic interaction of propylene glycol vehicle and delta-9-tetrahydrocannabinol.** Research Communications in Chemical Pathology and Pharmacology. 14(4):739-742, 1976.

The use of a propylene glycol vehicle (a mixture of 10% propylene glycol and 1% polysorbate (Tween) 80 in isotonic saline) for the intraperitoneal administration of delta-9-tetrahydrocannabinol (delta-9-THC) is examined. The apparent inhibition of delta-9-THC and ethanol metabolism demonstrated in this study by pretreatment with propylene glycol vehicle is similar to results obtained in other studies using propylene glycol itself. The cross-tolerance to delta-9-THC induced by propylene glycol vehicle pretreatment has not been previously reported. Because of the behavioral and metabolic interaction of this vehicle with delta-9-THC it is suggested that this vehicle not be used in studies in which delta-9-THC is repeatedly administered. 6 references. (Author abstract modified)

001386 Sprague, Gary L.; Craigmill, Arthur L. Midwest Research Institute, 425 Volker Blvd., Kansas City, MO 64110 **Ethanol and delta-9-tetrahydrocannabinol: mechanism for cross-tolerance in mice.** Pharmacology Biochemistry and Behavior. 5(4):409-415, 1976.

The pharmacological interaction between equipotent doses of ethanol and delta-9-tetrahydrocannabinol (THC) was evaluated in mice using rotarod performance as a measure of drug action. Tolerance to the effects of ethanol and THC as well as a symmetrical cross-tolerance between the two drugs was demonstrated. Ethanol elimination was not altered by previous administration of ethanol or THC. THC treatment had no effect on the metabolism or distribution of subsequently administered THC. Ethanol pretreatment altered both the distribution and hepatic metabolism of THC. No treatment regimens lowered whole brain levels of subsequently given THC or ethanol, suggesting that tolerance to ethanol or THC and cross-tolerance between the two drugs is not the result of lower brain concentrations. A vehicle effect was shown when treatment with a mixture of propylene glycol and Tween-80 altered the metabolism and the behavioral effects of subsequently administered THC. 30 references. (Author abstract modified)

001387 Stefanini, E.; Argiolas, A.; Gessa, G. L.; Fadda, F. Institute of Pharmacology, University of Cagliari, Italy **Effect of lithium on dopamine uptake by brain synaptosomes.** Journal of Neurochemistry (Oxford). 27(5):1237-1239, 1976.

The effects of lithium chloride on dopamine (DA) uptake into brain synaptosomes of rats were investigated. Lithium

added in vitro to synaptosomes isolated from the caudate nucleus, inhibited DA uptake. Following chronic administration of lithium chloride in vivo, dopamine uptake in vitro was enhanced. It is suggested that chronic lithium treatment stimulates a compensatory mechanism which overcomes its direct inhibitory effect on DA uptake. 18 references. (Author abstract modified)

001388 Stefanini, E.; Fadda, F.; Porceddu, M. L.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Effect of trazodone on brain dopamine metabolism.** Journal of Pharmacy and Pharmacology (London). 28(12):925-927, 1976.

The effect of trazodone on dopamine synthesis was studied in male Sprague-Dawley rats and male albino mice. Trazodone increased homovanillic acid (HVA) and dihydroxyphenylacetic acid (Dopac) concentrations in the brain in a dose dependent fashion, but brain dopamine levels were unaffected. Brain HVA and Dopac concentrations peaked at 1 h, and returned to normal by 3 h. Naloxone, 1mg/kg, failed to prevent the rise in brain HVA. Trazodone appears to share with butyrophenone and phenothiazine derivatives and narcotic analgesics the capacity of increasing brain dopamine metabolites. However, trazodone does not seem to cause catalepsy. 27 references.

001389 Stefano, George B.; Catapane, Edward; Aiello, Edward. Dept. of Biological Sciences, New York Community College, Brooklyn, NY 11201 **Dopaminergic agents: influence on serotonin in the molluscan nervous system.** Science. 194(4264):539-541, 1976.

The dopamine (DA) content of neurons in a representative mollusk, *Mytilus edulis*, was altered by selective drug treatments, and changes in the concentrations of serotonin (5-hydroxytryptamine, 5-HT) and DA were observed. Treatment with 6-hydroxydopamine, (6-OHDA) or with alpha-methyl-p-tyrosine decreased DA and increased 5-HT in the nervous system. Treatment with DA decreased 5-HT concentrations and prevented the effect of 6-OHDA. The 5-HT concentration appears to be determined in part by the concentration of DA. 17 references. (Author abstract modified)

001390 Stockard, J. J.; Myers, R. R.; Jones, T. A.; Bickford, R. G. no address **Modification of anesthetic-induced epileptiform EEG activity by experimental alterations of reticulo-cortical drive.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 41(6):651, 1976.

At a meeting of the Western EEG Society in San Antonio in February 1976, results of a study on modification of anesthetic induced epileptiform EEG activity by experimental alterations of the reticulocortical drive in cats using enflurane, isoflurane, fluorene or diethyl ether were reported. Four lines of evidence suggest that ascending reticular influences modulate the cerebral irritative effects of ether anesthetics: 1) EEG and multiple unit activity recordings indicated a close inverse correlation between tonic neuronal activity in the midbrain reticular formation (MRF) and epileptiform activity in limbic structures and neocortex; 2) electrical stimulation of the MRF decreased seizure activity of enflurane and isoflurane and increased seizure concentration of ether and fluorene; 3) reversible cryogenic cooling of the MRF enhanced enflurane induced irritative effects; and 4) generalized electrographic seizure activity equilibrated at subepileptogenic concentrations of fluorene and enflurane. Depression of reticulocortical desynchronizing drive may account for the paradoxical increase in electrocortical irritation caused by some CNS depressants in patients given enflurane.

001391 Stone, C. J.; Forney, R. B. Department of Toxicology, Indiana University School of Medicine, Indianapolis, IN **Toxicology of phencyclidine in mice.** *Toxicology and Applied Pharmacology*. 37(1):164, 1976.

An investigation was carried out to determine the effect of phencyclidine (PCP) on ethanol sleep time and hexobarbital sleep time and to examine the disappearance rate of PCP in whole mouse homogenates and various tissues. Loss of righting reflex, or sleep time, was measured after administration of a hypnotic dose of sodium hexobarbital or ethanol to mice pretreated with various doses of PCP and a regression line was fitted to the data. In both cases, regression analysis indicated the existence of a significant dose/response relationship. In the disappearance study, it was found that the half-life of PCP in whole mouse homogenates is 37.5 min. Disappearance rates were also studied in lung, liver, and brain. (Author abstract modified)

001392 Stone, T. W. Department of Physiology, University of Aberdeen, Marischal College, Aberdeen AB9 1AS, Scotland **Is glutamic acid the pyramidal tract neurotransmitter?.** *Experientia* (Basel). 32(5):581-583, 1976.

Studies were carried out using the amino acid antagonist 1-hydroxy-3-amino-pyrrolidone-2 (HA-966) to determine whether an excitatory amino acid could be involved in neurotransmission for fine movements of distal limb muscles and modulation of sensory information reaching higher centers such as the cerebral cortex. Applied by microiontophoresis, HA-966 antagonized excitation by glutamic acid but not by acetylcholine of neurones in the rat cuneate nucleus. HA-966 blocked the short latency excitation of cuneate neurones following stimulation of the pyramidal tract on 28 of 40 cells. Thus, glutamate or a related amino acid may be the neurotransmitter released by pyramidal tract neurones. 23 references. (Author abstract modified)

001393 Sugrue, Michael F.; Goodlet, Ian; Mireylees, Stewart E. Department of Pharmacology, Organon Scientific Development Group, Organon Laboratories Limited, Newhouse, Lanarkshire ML1 5SH, Scotland **On the selective inhibition of serotonin uptake in vivo by Org 6582.** *European Journal of Pharmacology* (Amsterdam). 40(1):121-130, 1976.

The effect of Org 6582 similar to a selective inhibitor of serotonin (5-HT) tricyclic antidepressants in blocking the ability of p-chloroamphetamine to decrease rat brain levels of serotonin in vivo was studied. Org 6582 was twice as potent as fluoxetine, 5 times more potent than chlorimipramine, and 14 times more potent than desipramine in blocking the ability of p-chloroamphetamine to lower 5-HT content in rat brains. It also decreased 5-HT brain turnover and lowered brain levels of 5-hydroxyindole acetic acid (5-HIAA). Org 6582 had no effect on the ability of 1-metraminol and 6-hydroxydopamine to lower heart noradrenaline levels and on the ability of intravenicularly administered 6-hydroxydopamine to lower brain noradrenaline levels or brain dopamine content. Org 6582 also had no effect on steady state levels or on turnover of noradrenaline or dopamine in rat brain. The results seem to indicate that Org 6582 is a potent inhibitor of 5-HT uptake, probably by competitive inhibition at synaptosomes, while it has no apparent effect on the uptake of both noradrenaline and dopamine. 31 references. (Author abstract modified)

001394 Sun, Albert Y. Sinclair Comparative Medicine Research Farm, University of Missouri, Columbia, MO 65201 **Alcohol-membrane interaction in the brain: norepinephrine release.** *Research Communications in Chemical Pathology and Pharmacology*. 15(4):705-719, 1976.

The effects of ethanol on release of norepinephrine (NE) from synaptosomal particles isolated from mouse brain were studied in vitro. Low concentrations of ethanol decreased synaptosomal NE release but higher concentrations of ethanol increased synaptosomal NE release. The NE release process was stimulated by potassium ion and calcium ion but inhibited by sodium ion and acetylcholine. It is suggested that the biphasic response of NE release to various concentrations of ethanol may be mediated by an effect of ethanol on active cation transport systems, in particular calcium ion transport. 29 references. (Author abstract modified)

001395 Symes, A. L.; Lal, S.; Sourkes, T. L. Department of Psychiatry, Montreal General Hospital, Montreal, P.Q., Canada **Time-course of apomorphine in the brain of the immature rat after apomorphine injection.** *Archives internationales de Pharmacodynamie et de Therapie* (Ghent). 223(2):260-264, 1976.

The behavioral effects induced by single doses of apomorphine and the time course of the drug in the brain were compared in 7-day-old rats and young adult rats. In the adult animals, continuous stereotyped behavior (SB) commenced within 1 to 2 min. and was no longer present at 75 min. The peak concentration of apomorphine was present at 5 min and then declined exponentially; only trace amounts were present at 90 min. In the immature rat, apomorphine induced an initial phase of intermittent locomotion lasting about 10 min. after which the rats appeared sedated. Intermittent SB emerged 60 to 180 min. after injection and terminated 150 to 180 min. after injection. The peak brain concentration was present at 10 minutes. Significant amounts of apomorphine were still present in the brain at 150 min. and trace amounts were evident at 180 min. The reason for the delayed onset of SB in the immature rat is unclear. It is suggested that the longer half-life may be related to incomplete development of the enzyme systems metabolizing apomorphine in the immature animal. 16 references. (Author abstract modified)

001396 Tanjasiri, Pornpun; Kozbur, Xenia; Florsheim, Warner H. Medical Research Service, U.S. Veterans Administration Hospital, Long Beach, CA 90822 **Somatostatin in the physiologic feedback control of thyrotropin secretion.** *Life Sciences* (Oxford). 19(5):657-660, 1976.

The addition of antiserum against Somatostatin (SRIF) to a culture of dispersed rat pituitary cells incubated in the presence of hypothalamic tissue enhanced thyrotropin (TSH) secretion into the medium. It is concluded that the results indicate that SRIF is normally secreted in amounts sufficient to affect TSH secretion. It is also suggested that SRIF may be the agent responsible for the unexplained rapid termination of TSH secretion by thyrotrophs which have been activated by Thyrotropin Releasing Factor (TRF). 16 references. (Author abstract modified)

001397 Tassin, J. P.; Cheramy, A.; Blanc, G.; Thierry, A. M.; Glowinski, J. Groupe NB INSERM U. 114, Collège de France, F-75231 Paris Cedex 5, France **Topographical distribution of dopaminergic innervation and of dopaminergic receptors in the rat striatum. I. Microestimation of (3H)dopamine uptake and dopamine content in microdiscs.** *Brain Research* (Amsterdam). 107(2):291-301, 1976.

Topographical variations in the uptake of 3H-dopamine (DA) and in the endogenous content of DA in the striatum of the rat were investigated using microdiscs which were punched out in serial sections. 3H-DA uptake was measured in sucrose homogenates prepared from microdiscs punched out from

frozen slices. The uptake was similar to that observed in fresh tissues. It was unaffected by desmethylimipramine, inhibited by benztropine and no longer detectable after 6-hydroxydopamine induced degeneration of the nigrostriatal dopaminergic pathway. Both 3H-DA uptake and DA content decreased regularly from the rostral to the caudal part of the structure. In contrast, no important differences could be found in the dorsoventral plane. It is suggested that the extent of dopaminergic innervation is heterogeneous within the structure. 21 references. (Author abstract modified)

001398 Taylor, D.; Nathanson, J.; Hoffer, B.; Olson, L.; Seiger, A. National Institute of Mental Health, Saint Elizabeths Hospital, Washington DC 20032 **Lead blockade of noradrenergic inhibition in cerebellar Purkinje neurons.** (Unpublished paper). SMR, National Institute of Mental Health, 1976.

The effects of the lead ion on the depression of spontaneous discharge of Purkinji (P) cells produced by iontophoresis of norepinephrine (NE) was investigated. Iontophoresis of lead ion reliably antagonized NE responses in over 80% of the P cells studied. Spontaneous discharge rate was either unaffected or slightly elevated at lead ion levels that almost completely blocked NE. Stimulation of parallel fibers or iontophoresis of acetylcholine (ACh) excited P cells. No antagonism was seen between lead ion and ACh or parallel fiber excitations. Basket cell inhibition, believed to be mediated by GABA, was similarly not reduced. It is suggested that specific blockade of brain catecholamine receptors may partially underlie the CNS toxicity due to lead administration. (Author abstract modified)

001399 Taylor, Dorothy; Ho, Beng T. Texas Research Institute of Mental Sciences, Houston, TX 77030 **Effect of short-term and long-term treatment with cocaine on rat brain tryptophan hydroxylase.** Research Communications in Chemical Pathology and Pharmacology. 15(4):805-808, 1976.

The effects of long-term and short-term treatment with cocaine on rat brain tryptophan hydroxylase were examined. Short-term (5 days) cocaine treatment inhibited the soluble tryptophan hydroxylase, while the particulate enzyme was essentially unchanged. Long-term (45 days) cocaine treatment resulted in an increased activity of the particulate enzyme and a return to normal of the soluble enzyme activity. It is suggested that the initial effect of cocaine may be stimulation of serotonin (5-HT) receptors and that the increase in particulate tryptophan hydroxylase activity during long-term cocaine treatment may be a biochemical compensatory mechanism to control 5-HT receptor stimulation. 8 references. (Author abstract modified)

001400 Terasawa, Ei; Goldfoot, David A.; Davis, Gary A. Wisconsin Regional Primate Research Center, Madison, WI 53706 **Pentobarbital inhibition of progesterone-induced behavioral estrus in ovariectomized guinea pigs.** Brain Research (Amsterdam). 107(2):375-383, 1976.

The relationships between estrus behavior, pentobarbital and progesterone were investigated in ovariectomized guinea-pigs. Pentobarbital injections given 8 h before progesterone had no effect on latency to the first lordosis or on other parameters of estrus behavior. However, pentobarbital delayed the onset of heat in estrogen treated ovariectomized guinea-pigs when given shortly before, or simultaneously with progesterone. The delay was directly related to the length of time the animals remained asleep after the progesterone injection. In animals receiving progesterone before receiving pentobarbital, the

latency of recovery from anesthesia to the first display of lordosis was shorter than in the other pentobarbital groups. The duration of heat was unaffected by the anesthetic for all groups mentioned. In animals which received pentobarbital after they were already in heat, pentobarbital injection terminated heat and abolished it completely. Gross hypothalamic uptake of progesterone was not influenced by pentobarbital administration. It is tentatively concluded that an incubation period is necessary for progesterone to mediate the display of estrus behavior in the guinea-pig in addition to the time necessary for neural uptake. 34 references. (Author abstract modified)

001401 Thiercelin, J. F.; Jacquot, C.; Rapin, J. R.; Cohen, Y. Laboratoire de Pharmacodynamie, UER de Chimie Therapeutique, Universite de Paris-Sud, F-92290 Chatenay Malabry, France **/Pharmacokinetics of DL-norephedrine 14C in the rat./ Pharmacocinetique de la DL-norephedrine 14C chez le rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 220(1):153-163, 1976.

Distribution of DL-norephedrine and of its metabolites was studied in male Wistar mice and male Charles River rats. The mice, weighing 20g, were given C14 labeled norephedrine HCl i.v. and were sacrificed. Cross-sections of the whole mouse were studied. At 2 min, radioactivity was concentrated in the liver, kidneys, digestive organs, and periorcular area, and at 15 min, radioactivity had also accumulated in the salivary gland. By 2 to 4 hr, radioactivity had reached negligible levels except in the urinary tract. Male rats averaging 260g in weight were given labeled norephedrine and were exsanguinated. The adrenals, spleen, lungs, heart, and brain were removed along with heparinized blood, and the radioactivity measured. At 5 min, radioactivity was found in decreasing order in the lung, adrenals, spleen, heart, brain, and plasma, and by 15 min, rapid elimination had occurred from all of these tissues except the brain. Other rats averaging 200g were given the labeled norephedrine, and their urine and feces were collected. The urinary metabolites were separated by paper chromatography. Norephedrine was found to be transformed into alpha-methyloctopamine (p-hydroxynorephedrine). Fecal excretion was negligible. Uptake of alpha-methyloctopamine was highest in organs rich in adrenergic nerve endings, such as the heart, adrenals, and spleen, thus confirming its role as a false neurotransmitter. 19 references.

001402 Thoa, N. B.; Tizabi, Y.; Kopin, I. J.; Maengwyn-Davies, G. D. Laboratory of Clinical Sciences, Building 10, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20014 **Alterations of mouse adrenal medullary catecholamines and enzymes in response to attack: effect of pre- and post-treatment with phenobarbital.** Psychopharmacology (Berlin). 51(1):53-57, 1976.

The time course of changes in levels of adrenal norepinephrine (NE), epinephrine (EPI), tyrosine hydroxylase (TH) and phenylethanolamine-N-methyltransferase (PNMT) were determined following exposure of mice to the anxiety stress of daily attacks by aggressor mice. The effects of phenobarbital administered prior to the attacks or after the attacks were also examined. TH was increased after two exposures and remained elevated through 14 daily exposures to attack. PNMT was increased after two exposures and further increased after 14 daily exposures. No changes in NE or EPI occurred within the first 4 days but substantial increases occurred after 7 days of daily exposure. Following 1 week of daily exposure, EPI levels and PNMT activities returned to normal after 4 days but NE levels and TH activities returned

to normal only after 1 week. Phenobarbital prevented the biochemical changes when given 2 h prior to each daily attack but was ineffective when given immediately after each attack. 18 references. (Author abstract modified)

001403 Thomsen, Klaus. Psychopharmacology Research Unit, Psychiatric Hospital in Aarhus, DK-8240 Risskov, Denmark. **Renal elimination of lithium in rats with lithium intoxication.** *Journal of Pharmacology and Experimental Therapeutics*. 199(3):483-489, 1976.

The relationship between urine flow, lithium clearance and sodium clearance was studied in rats given lithium in amounts leading to inhibition of distal reabsorption of water and sodium. Maximum inhibition of water reabsorption was reached at serum lithium concentrations of about 1mM. At higher serum lithium levels the rats developed intoxication due to a lowering of lithium clearance. The intoxication was characterized by a proportional decrease of urine flow and lithium clearance. The decrease of urine flow and lithium clearance was not related to changes of sodium clearance. It is posited that lithium is reabsorbed in the proximal tubules in parallel with sodium and that the lowering of lithium clearance is due to increased fractional proximal reabsorption of lithium and sodium compensatory to inhibition of the distal reabsorption of sodium. 20 references. (Author abstract modified)

001404 Trulson, Michael E.; Ross, Christopher A.; Jacobs, Barry L. Department of Psychology, Princeton, University, Princeton, NJ 08540. **Behavioral evidence for the stimulation of CNS serotonin receptors by high doses of LSD.** *Psychopharmacology Communications*. 2(2):149-164, 1976.

The effects of lysergic acid diethylamide (LSD) on a behavioral syndrome which reflects increased activation of central serotonin receptors were studied in rats. A marked supersensitivity to LSD was observed in rats whose serotonin nerve terminals had been selectively destroyed, and a dramatic tolerance to LSD was observed following repeated administration of LSD to normal rats. It is concluded that direct evidence has been provided that LSD can stimulate CNS serotonin receptors to a degree which markedly affects behavior. 32 references. (Author abstract modified)

001405 Tyce, Gertrude M. Depts. of Physiology and Biophysics, Mayo Clinic and Foundation, Rochester, MN 55901. **The effect of L-DOPA and an inhibitor of peripheral decarboxylation on glucose metabolism in brain.** *Journal of Neurochemistry* (Oxford). 27(6):1397-1403, 1976.

The effects of L-DOPA and a peripheral decarboxylation inhibitor on glucose metabolism in rat brain were investigated using labeled glucose. Three groups of rats were used: 1) rats that had been injected with L-DOPA (200mg/kg) 28 minutes earlier; 2) rats that had been similarly injected with L-DOPA and also with N-(D,L-seryl)-N'-(2,3,4-trihydroxybenzyl)hydrazine, an inhibitor of L-aromatic amino acid decarboxylase, 30 minutes before the L-DOPA; and 3) appropriate controls. The flux of radioactive carbon label from glucose in plasma to those amino acids that are in equilibrium with the tricarboxylic acid cycle intermediates was reduced by treatment with L-DOPA and reduced further by treatment with L-DOPA and the decarboxylase inhibitor. Concentrations of glucose in brain and in plasma were increased after treatment with L-DOPA. These increases were attenuated if the inhibitor was given before the L-DOPA. After treatment with L-DOPA, there were decreases in the concentration of aspartate, tryptophan, and tyrosine in brain. After the administration of L-DOPA and the decarboxylase inhibitor, the concentrations in

brain of alanine, glutamate, tyrosine, and phenylalanine were greater, and the concentrations of aspartate, leucine, lysine, histidine, arginine, and tryptophan were less than in control rats. 32 references. (Author abstract modified)

001406 Uhl, George R.; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205. **Regional and subcellular distributions of brain neurotensin.** *Life Sciences* (Oxford). 19(12):1827-1832, 1976.

The regional and subcellular distribution of neurotensin were determined using a newly developed radioimmunoassay for this central nervous system tridecapeptide. Neurotensin immunoreactivity in calf brain is high in the hypothalamus and basal ganglia, unevenly distributed through the cerebral cortex, and low in cerebellar cortex and cerebral white matter. Subcellular fractionation of rat hypothalamus reveals a strong association of neurotensin immunoreactivity with synaptosomal and microsomal fractions. These data, taken along with previously described high affinity selective brain membrane receptor binding, are consistent with a neurotransmitter candidate role for neurotensin in the brain. 13 references. (Author abstract)

001407 Uspenskiy, A. Ye.; Korobov, N. V. Pervyy Moskovskogo meditsinskogo instituta im. I. M. Sechenova, Moscow, USSR. **Facilitation of effects of L-dopa by alpha-methyl-dopa.** *Obusilenii efektoy L-dofa na fone alfa-metil-dofa. Byulleten' Eksperimental'noy Biologii i Meditsiny* (Moskva). 81(3):314-316, 1976.

The influence of alpha-methyl-dopa on central and peripheral effects of L-dopa is analyzed. In male mice, alpha-methyl-dopa increased the duration of excitation induced by L-dopa and facilitated the anticonvulsant effect of L-dopa in mice pretreated with reserpine or haloperidol. In cats, alpha-methyl-dopa given 30 minutes prior to L-dopa diminished the influence of L-dopa on blood pressure and contraction of the nictitating membrane. Given 4 to 6 hours before L-dopa, alpha-methyl-dopa enhanced the reaction of blood pressure and contraction of nictitating membrane induced by L-dopa or dopamine. 12 references.

001408 van Dorsser, W.; Dresse, A. Institut de Therapeutique Experimentale, Universite de Liege, 32, Boulevard de la Constitution, B-4020 Liege, Belgium. **Interaction of tricyclic antidepressants with noradrenaline and 5-hydroxytryptamine on peripheral preparations in the rat.** *Interaction des antidepressants tricycliques avec la noradrenaline et la 5-hydroxytryptamine sur des preparations peripheriques chez le rat. Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 220(1):164-176, 1976.

The effect of eight substances with antidepressant effect was studied on the response of the vas deferens and the blood pressure to noradrenaline and the response of the uterus to serotonin in rats. The eight substances were amitriptyline, protriptyline, imipramine, desipramine, clomipramine, LM-208 (a new dibenzazepine), orphenadrine, and its demethylated derivative, tofenazine. Male Wistar rats weighing 200 to 300g were used. Blood pressure was measured in female Wistar rats weighing 200 to 400g. Norepinephrine was given i.v. Only protriptyline and desipramine substantially potentiated the response of the vas deferens to norepinephrine, while amitriptyline was inhibitory. Protriptyline and desipramine potentiated the effect of noradrenaline on blood pressure the most, while all antidepressants prolonged the effect of noradrenaline. All the drugs inhibited the effect of serotonin on contraction of the uterus. 21 references.

001409 Vargas, F.; Erij, D. Deptos. de Neurociencias y Fisiologia, Centro de Investigacion, I.P.N., Mexico 14, D.F., Mexico The effects of harmaline on GABA fluxes in pinched-off nerve endings. *Brain Research (Amsterdam)*. 113(3):611-615, 1976.

The effect of harmaline on the uptake of amino acids by cells of the nervous system was investigated in isolated rat brain synaptosomes. Harmaline inhibits the uptake of gamma-aminobutyric acid. The effects of harmaline were compared with the effects of ouabain on the uptake and efflux of GABA from synaptosome. Harmaline inhibits a greater fraction of total amino acid uptake than does ouabain. Harmaline interacts with the amino acid transport site independently of the inhibition of sodium/potassium/adenosine/triphosphatase. It is suggested that the action of harmaline on amino acid uptake cannot be ascribed only to the blockade of the sodium pump. 12 references.

001410 von Stralendorff, B.; Ackenheil, M.; Zimmermann, J. Psychiatrische Klinik der Universität München, Nussbaumstrasse 7, D-8000 Munich 2, Germany /Acute and chronic effect of caripramine, clozapine, haloperidol, and sulpiride on metabolism of biogenic amines in the rat brain./ Akute und chronische Wirkung von Caripramin, Clozapin, Haloperidol und Sulpirid auf den Stoffwechsel biogener Amine im Rattengehirn. *Arzneimittel-Forschung (Aulendorf)*. 26(6):1096-1098, 1976.

The effect of haloperidol, clozapine, sulpiride, and caripramine on the metabolism of biogenic amines was studied in male Sprague-Dawley rats weighing 180 to 200g. Dosage was: 5mg/kg haloperidol, 50mg/kg clozapine, 100mg/kg sulpiride, and 50mg/kg caripramine, all given i.p. at 6 p.m. The animals were decapitated at 8 p.m. 3-Methoxy-4-hydroxyphenylglycol (MHPG), homovanillic acid (HVA), and 5-hydroxyindoleacetic acid (5-HIAA) were determined by gas chromatography. Haloperidol caused catalepsy; the other three drugs did not. Haloperidol and clozapine markedly decreased motor activity on the 1st day, but had no effect on the 11th day of chronic treatment. The other drugs did not affect motor activity on either the 1st or 11th days. All four drugs significantly increased MHPG levels after a single dose, and MHPG levels dropped on the 11th day. 5-HIAA levels were increased after chronic treatment with haloperidol, sulpiride, and caripramine, but not clozapine. All four drugs caused increases in HVA. The haloperidol treated rats developed a tolerance to dopamine turnover. 18 references.

001411 Wahlstrom, Goran. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden The interaction between spontaneous convulsions and tolerance to hexobarbital in the abstinence after chronic barbital treatments in the rat. *Life Sciences (Oxford)*. 19(12):1817-1826, 1976.

The interaction between spontaneous convulsions and tolerance to hexobarbital in the abstinence after chronic barbital treatments in the rat was studied. In two experiments tolerance was induced by treatment with barbital in the drinking water. Two treatment periods with a total duration of about 55 weeks were given in each experiment. In the abstinence after the second treatment period tolerance was measured with a hexobarbital threshold method. It was found that the convulsion, which is regarded as a sign of physical dependence, can reduce the tolerance to hexobarbital in the abstinence after chronic barbital treatments. It is theorized that the convulsion could not only be the sign but also the means to at least temporarily decrease physical dependence. 12 references. (Author abstract modified)

001412 Waldmeier, P. C.; Maitre, L. Research Department, Pharmaceuticals Division, Ciba-Geigy Limited, Basel, Switzerland Clozapine: reduction of the initial dopamine turnover increase by repeated treatment. *European Journal of Pharmacology (Amsterdam)*. 38(1):197-203, 1976.

The levels of homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC) in rat striatum after acute and 10 day administration of clozapine, thioridazine, haloperidol and chlorpromazine were estimated, and the levels of HVA in the mesolimbic area were investigated on the clozapine and haloperidol treatment, in a study of a characteristic feature of a dopamine receptor blocker, namely tolerance development with regard to the elevation of HVA. With all these neuroleptics, the levels of both dopamine metabolites were reduced after a 20 day treatment as compared to acute administration, sometimes almost to control levels. With clozapine, however, such a reduction occurred only with the higher dose of 100mg/kg p.o., acting for a period longer than 24 hours. This tolerance phenomenon was also observed with clozapine and haloperidol in the mesolimbic area. It is concluded that clozapine is not qualitatively different from classical neuroleptics with respect to development of biochemical tolerance. 26 references. (Author abstract modified)

001413 Waldmeier, P. C.; Maitre, L. Department Forschung, Division Pharma Ciba-Geigy AG, CH-4002 Basel, Switzerland Comparison of short and long-lasting effects of pargyline on cerebral dopamine metabolism. *Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin)*. 294(2):133-140, 1976.

The influence of the time interval between pargyline pretreatment and L-dopa administration on the metabolism of L-dopa in the rat brain was investigated. After pargyline pretreatment, the half-lives of recovery of striatal monoamine oxidase (MAO) activity and normal endogenous concentrations of homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC) in striatum ranged from 9 days to 14 days. A marked accumulation of methoxytyramine (MT) and dopamine (DA) occurred; recovery from this effect had a half-life of 15 h to 19 h. The only labelled deaminated metabolite of dopamine in the brain after iv administration of radiolabelled DOPA was HVA, which was strongly reduced 2 h after pargyline but normalized approximately 24 h after pargyline. When animals were pretreated with pargyline at various times up to 21 days, a second injection of pargyline 1.5h before H-dopa restored the increase in MT and DA observed with a single treatment with pargyline 1.5h before the labelled precursor. The threshold dose of pargyline for producing this short-term effect was about 10 times higher than that for an overall MAO inhibiting effect. It is suggested that an additional form of MAO exists which has a rapid turnover, a marked capacity to deaminate DA or MT, and a greater resistance to inhibition by pargyline than cerebral MAO in general. 18 references. (Author abstract modified).

001414 Wauquier, Albert; Niemegeers, Carlos J. E. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, Beerse, Belgium Restoration of self-stimulation inhibited by neuroleptics. *European Journal of Pharmacology (Amsterdam)*. 40(1):191-194, 1976.

The restoration of brain self-stimulation inhibited by neuroleptics in rats was studied. Pimozide induced inhibition of lever pressing for brain stimulations in the lateral hypothalamic area was differentially restored by dextimide, cocaine, nomifensine and amphetamine while pibedil and apomorphine were without effect. The chlorpromazine induced inhibition was not antagonized by dextimide but was completely

reversed by amphetamine and nomifensine. The results suggest that noncompetitive antagonism anticholinergics or drugs which enhance endogenous neurotransmission by increased release or uptake blockade may be able to reverse neuroleptic induced inhibition of self-stimulation more effectively than receptor antagonists. 10 references. (Author abstract modified)

001415 Weinstock, Marta; Cohen, Dvora. Department of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel **Tricyclic antidepressant drugs as antagonists of muscarinic receptors in sympathetic ganglia**. *European Journal of Pharmacology* (Amsterdam). 40(2):321-328, 1976.

The effects of desipramine, imipramine, chlorimipramine, iprindole and viloxazine on contractions of the nictitating membrane produced by the ganglion stimulants 4-(meta-chlorophenylcarbamoyloxy)-2-butyltrimethyl ammonium chloride (McN-A-343), dimethylphenylpiperazinium (DMPP) or 5-hydroxytryptamine (5-HT) were investigated in cats. The ganglionic effects of McN-A-343 but not those of DMPP were antagonized in a dose related manner by 2 microgram to 10 microgram doses of each of the antidepressants. Chlorimipramine and imipramine were more potent antagonists of 5-HT than of McN-A-343, while viloxazine was much less potent and iprindole was inactive against 5-HT. No correlation was found between the dose of each drug which blocked the effects of McN-A-343 and that required to potentiate the nictitating membrane responses to intraarterial administration of noradrenaline. It is concluded that clinically effective antidepressant agents can block muscarinic receptors in neural tissue. 34 references. (Author abstract modified)

001416 Wenzlik, R.; Klinger, W. Aus dem Institut für Pharmakologie und Toxikologie der Friedrich-Schiller-Universität, Jena, DDR **The effects of adrenaline and glucose on hexobarbital sleeping time and on hexobarbital blood levels in the rat. Seitenlagenzeit und Aufwachkonzentration im Blut nach Hexobarbital unter Einwirkung von Glukose und Adrenalin bei Ratten beiderlei Geschlechts**. *Archives internationales de Pharmacodynamie et de Therapie* (Ghent). 223(1):155-161, 1976.

The effects of adrenalin and glucose administered by various routes on hexobarbital sleeping time and on blood concentrations of hexobarbital at awakening were studied in rats. Sleeping times in male and female rats were prolonged after the simultaneous i.p. administration of adrenaline and hexobarbital sodium. The blood concentration of hexobarbital at awakening was unchanged in male rats, but in females the concentration was decreased. When adrenaline was given s.c., no change in sleeping time was observed in either sex, but the blood concentration of hexobarbital for both was decreased. Glucose, given p.o. or i.p., had no influence on sleeping times or on hexobarbital concentrations. The hexobarbital concentration at awakening was higher in female than in male rats. 14 references. (Author abstract modified)

001417 Westerink, Ben H. C.; Korf, Jakob. Laboratory for Pharmaceutical and Analytical Chemistry, Dept. of Clinical Chemistry, Groningen University, Groningen, The Netherlands **Acidic dopamine metabolites in cortical areas of the rat brain: localization and effects of drugs**. *Brain Research* (Amsterdam). 113(2):429-434, 1976.

Confirming recent biochemical and histochemical findings, this study shows the presence of dopaminergic metabolism in certain cortical regions of the rat brain. Various drug treatments including haloperidol or haloperidol combined with probenecid, suggest that dopaminergic metabolism in the fron-

tal cortex shows similarities to that in mesolimbic tissue. 18 references.

001418 Westerink, Ben H. C.; Korf, Jakob. Laboratory for Pharmaceutical and Analytical Chemistry, Department of Clinical Chemistry, Antonius Deusinglaan 2, Groningen, The Netherlands **Effects of drugs on the formation of homovanillic acid in the rat retina**. *European Journal of Pharmacology* (Amsterdam). 40(1):175-178, 1976.

The effects of drugs on the formation of homovanillic acid (HVA) in the rat retina and the corpus striatum were studied. Neuroleptics such as clozapine, cis-flupenthixol and haloperidol induced similar increases in HVA levels, while the transomer of flupenthixol was inactive in both brain and retina. Apomorphine decreased HVA levels in both brain and retina while amphetamine decreased HVA formation in the retina without changes in the corpus striatum. Probenecid caused a similar HVA rise in both brain and retina while morphine and oxotremorine induced an HVA rise in the corpus striatum but not in the retina. The results suggest that in the corpus striatum and retina, comparison of dopamine metabolism based on HVA levels could be used to differentiate between drugs whose action is dependent or independent of the connections of dopaminergic neurons with other neuronal systems. 10 references. (Author abstract modified)

001419 Westerink, Ben H. C.; Korf, Jakob. Laboratory of Pharmaceutical and Analytical Chemistry, Department of Clinical Chemistry, Antonius Deusinglaan 2, Groningen, The Netherlands **Comparison of effects of drugs on dopamine metabolism in the substantia nigra and the corpus striatum of rat brain**. *European Journal of Pharmacology* (Amsterdam). 40(1):131-136, 1976.

The effects of various drugs on dopamine metabolism in the substantia nigra and corpus striatum of rat brain were studied. Changes in dopamine (DA) utilization or synthesis by apomorphine, chloral hydrate, haloperidol, morphine, oxotremorine, pargyline, probenecid and promethazine were measured as changes in the metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA). The time/effect curves for the substantia nigra showed an initial rapid HVA rise not observed in the corpus striatum. Promethazine treatment caused a small but significant HVA rise in the substantia nigra only while chloral hydrate, morphine and oxotremorine produced a similar increase in DOPAC and HVA levels in the substantia nigra and the corpus striatum. Haloperidol caused only a small change in DOPAC and HVA levels in the substantia nigra but significant increases were seen in the corpus striatum, while apomorphine caused an HVA decrease in both structures. The results suggest the presence of a dopaminergic receptor in the substantia nigra and that the dopamine present in the substantia nigra may have an important role in the function of dopaminergic nerve cells. 21 references. (Author abstract modified)

001420 Westerink, Ben H. C.; Korf, Jakob. Department of Clinical Chemistry, Antonius Deusinglaan 2, Groningen, The Netherlands **Regional rat brain levels of 3,4-dihydroxyphenylacetic acid and homovanillic acid: concurrent fluorometric measurement and influence of drugs**. *European Journal of Pharmacology* (Amsterdam). 38(2):281-291, 1976.

A concurrent semiautomatic fluorometric assay technique for 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) is described. DOPAC and HVA were measured in the corpus striatum, nucleus accumbens and olfactory tubercle of the rat, under normal conditions and after treatment with

amphetamine, apomorphine, clozapine, haloperidol, morphine, oxotremorine, pargyline, probenecid, sulpiride and thioridazine. Clozapine, morphine, sulpiride and oxotremorine induced the most pronounced rise of dopamine (DA) metabolites in the nucleus accumbens. Probenecid produced a DOPAC accumulation in the nucleus accumbens. Striking differences were observed between the DOPAC/HVA ratios in the different structures of control animals. The concurrent assay enables a rapid screening of the action of drugs in regional DA metabolism. 41 references. (Author abstract modified)

001421 Widelitz, Martin M.; Coryell, Marlene R.; Widelitz, Howard; Avadhani, Narayan G. Research and Development Service, Veterans Administration Hospital, Coatesville, PA 19320 **Effects of amphetamine administration in vivo on in vitro protein synthesizing system from rat brain.** *Journal of Neurochemistry* (Oxford). 27(2):471-475, 1976.

A highly active in vitro protein synthesizing system (S-28) has been prepared from rat brain for use in investigating the effects of amphetamine administration in vivo on the in vitro system. Experimentation showed that poly(U)-dependent 3H-labeled phenylalanine incorporation by brain S-28 system was significantly inhibited by D-amphetamine. The extent of inhibition by amphetamine was significantly higher than by other biogenic amines such as dopamine and serotonin. At the 100 micrograms level of amphetamine incorporation, the inhibition was about 70%. Experiments with ribosomes and soluble enzymes from control and amphetamine treated systems indicated that the observed inhibition may be due to the effect of the drug on the ribosomes. Kinetic analysis of the reaction mixture in the presence as well as absence of D-amphetamine indicate that this sympathomimetic drug inhibits polysome formation in vitro. Results do not imply that inhibition of protein synthesis is the sole neurological effect of amphetamine causing psychotic behavior, although it appears that interference with protein synthesis is one of the biochemical effects of this drug which may be related to toxic psychosis. 25 references. (Author abstract modified)

001422 Wiesel, Frits-Axel; Alfredsson, Gunnel. Division of Neuropsychopharmacology, Department of Pharmacology, Karolinska Institutet, S-104 01 Stockholm, Sweden **The distribution and metabolism of chlorpromazine in rats and the relationship to effects on cerebral monoamine metabolism.** *European Journal of Pharmacology* (Amsterdam). 40(2):263-272, 1976.

The relationship between the distribution of chlorpromazine (CPZ) and its metabolites, monodemethylchlorpromazine and 7-hydroxychlorpromazine, in the brain and blood and the effects of the drug on dopamine (DA) metabolism in the striatum was investigated in rats. The time curves for increases in the DA metabolites dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in the striatum were similar to the curve for the CPZ concentration in the brain. The time curves for the levels of the CPZ metabolites did not show such a resemblance. It is suggested that unchanged CPZ is predominantly responsible for the acceleration of DA metabolism in the striatum. 33 references.

001423 Wong, David T.; Bymaster, Frank P. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **The comparison of fluoxetine and nisoxetine with tricyclic antidepressants in blocking the neurotoxicity of p-chloroamphetamine and 6-hydroxydopamine in the rat brain.** *Research Communications in Chemical Pathology and Pharmacology*. 15(2):221-231, 1976.

Elaboration of the central action of fluoxetine and nisoxetine in rats has been presented by showing the drugs' selective ability to prevent the loss of 5-hydroxytryptamine (5HT) and norepinephrine (NE) uptake after an intraperitoneal injection of p-chloroamphetamine (p-CA) or an intraventricular injection of 6-hydroxydopamine (6-OHDA), comparing results with those achieved with tricyclic antidepressants. After intraperitoneal administration of p-CA, fluoxetine prevented loss of 5HT uptake in synaptosomes of cerebral cortex. At a higher dosage of p-CA, fluoxetine did not prevent loss of NE uptake in synaptosomes of hypothalamus after intraventricularly administered 6-OHDA. Nisoxetine centrally protected NE uptake from the neurotoxic effect of 6-OHDA, but at a higher dosage it gave only 35% protection of 5HT uptake from the neurotoxic effect of p-CA. In comparison with the values of tricyclic antidepressants, both fluoxetine and nisoxetine are more potent and selective blockers of neurotoxicity resulting from the central actions of p-CA and 6-OHDA, respectively, in vivo. 15 references. (Author abstract modified)

001424 Yaksh, Tony L.; Yeung, Joseph C.; Rudy, Thomas A. School of Pharmacy, University of Wisconsin, Madison, WI 53706 **Systematic examination in the rat of brain sites sensitive to the direct application of morphine: observation of differential effects within the periaqueductal gray.** *Brain Research* (Amsterdam). 114(1):83-103, 1976.

An extensive mapping of the rat brain (403 sites) ranging from AP plus 8 to AP minus 3 revealed that the region showing maximum sensitivity to the intracerebral administration of morphine in the elevation of the nociceptive threshold lay within the periaqueductal gray. Analysis of the distribution of responsive sites indicated that the most active sites, those having the shortest latency of effect, were located within the ventrolateral aspect of the caudal periaqueductal gray. These antinociceptive actions of morphine were observed to be both dose dependent and reversible by the administration of naloxone. It was observed that microinjections of morphine could produce changes in the pinch withdrawal response which were distributed in a crude somatotopic fashion. Injections into the rostral aspect of the periaqueductal gray yielded a block of the pinch response in the rostral portions of the body, whereas such injections into the caudal periaqueductal gray always yielded a whole body analgesia. In the rostral sites, transient ipsilateral blocks of the pinch response were occasionally seen. It is suggested that morphine acting through the periaqueductal gray may actuate a potent supraspinal modulatory system related to the transmission of information derived from behaviorally aversive stimuli. 45 references. (Author abstract)

001425 Yarbrough, G. G. Merck Institute for Therapeutic Research, West Point, PA 19486 **TRH potentiates excitatory actions of acetylcholine on cerebral cortical neurones.** *Nature* (London). No. 5577:523-524, 1976.

Spontaneously active neurons, located between 750 micrometers and 1250 micrometers from the cortical surface, were studied to test the hypothesis that thyrotropin releasing hormone (TRH) would potentiate the excitatory actions of acetylcholine (ACh) on rat cortical neurons. Applications of TRH consistently enhanced the action of iontophoretically applied ACh. On 16 of 18 cells tested, TRH either potentiated the excitatory actions of regularly applied pulses of ACh or converted an inactive ejection current of ACh to a typical ACh excitation. Since a possible explanation for the ability of TRH to enhance ACh excitations while not affecting glutamate responses might be that of acetylcholinesterase inhibition, the interactions of

TRH and carbachol (not subject to degradation by acetylcholinesterase) were examined. On 11 of 13 cells tested, TRH potentiated the excitatory actions of carbachol. This effect of TRH on excitations produced by both ACh and carbachol was consistently brief in onset (sometimes occurring when the TRH and cholinergic agonist were applied simultaneously) and offset. TRH was not observed to have any direct effects on neuronal excitability of the restricted population of cells sampled with the ejection currents used, although it clearly and consistently enhanced the excitatory actions of ACh and carbachol. 9 references.

001426 Zakusov, V. V.; Porfirieva, R. P. Institut farmakologii AMN SSSR, Moscow, USSR /Influence of some productive tropines on absorption of noradrenaline by synaptic vesicles of the hypothalamus./ Vliyaniye nekotorykh proizvodnykh tropana na pogloshcheniye noradrenalina sinapticheskimi pusr'kami gipotalamusa. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 82(7):821-823, 1976.

The effect of productive tropines on absorption of noradrenaline by syntactic vesicles of the hypothalamus of the rat was investigated. The effect of cocaine was used as a standard, because of its relation to presynaptic blocking of the adrenaline mediator. Results show that beta morpholinopropionic acid tropine ester dihydrochloride, like cocaine, has a depressive effect on passive absorption of noradrenaline by synaptic vesicles of the hypothalamus in vitro. However, the effect depends on the concentration of noradrenaline in the incubation medium. 8 references.

001427 Ziance, Ronald J. Department of Pharmacology, School of Pharmacy, University of Georgia, Athens, GA 30602 Effect of propranolol on rat brain norepinephrine in vitro. Research Communications in Chemical Pathology and Pharmacology. 15(2):361-364, 1976.

The effects of propranolol on the release, uptake, and deaminative catabolism of norepinephrine (NE) in rat brain were demonstrated. At a low molar concentration range, 1-propranolol, dl-propranolol, and d-propranolol were equipotent to progressively inhibit the uptake of labeled NE into chopped rat cerebral cortex tissue. Similar concentrations of 1-propranolol and dl-propranolol, but not d-propranolol, significantly increased the amount of total deaminated catabolites (deaminated-O-methylated) of labeled NE, but smaller molar concentrations of the three substances were required to increase the release of labeled NE from rat brain in vitro. It appears that the effect of the propranolol isomers to inhibit NE uptake is not related to their beta-blocking action, but some local anesthetic action may be involved. 9 references. (Author abstract modified)

001428 Zieglansberger, W.; Fry, J. P.; Herz, A.; Moroder, L.; Wunsch, E. Department of Neuropharmacology, Max-Planck-Institute fur Psychiatrie, D-8 Munich 40, Germany. Enkephalin-induced inhibition of cortical neurones and the lack of this effect in morphine tolerant/dependent rats. Brain Research (Amsterdam). 115(1):160-164, 1976.

The effects of synthetic enkephalin applied microelectrophoretically to neurones in the cerebral cortex of the rat were examined in naive animals and in rats made tolerant/dependent to morphine. Enkephalin decreased the spontaneous firing rate of cortical neurones, but did not completely inhibit neuronal firing, and antagonized L-glutamate induced firing in naive rats. Prior application of naloxone completely blocked these effects of enkephalin. In morphine tolerant dependent rats, enkephalin did not inhibit glutamate

induced firing and when applied to spontaneously firing cells was either without effect or caused an increase in firing rate. This cross-tolerance between enkephalin and morphine suggests that future drugs based on the enkephalin peptides might be expected to have a tolerance/dependence liability. 20 references.

001429 Zieglansberger, W.; Bayerl, H. Department of Neuropharmacology, Max-Planck-Institute for Psychiatry, D-8 Munich 40, Germany The mechanism of inhibition of neuronal activity by opiates in the spinal cord of cat. Brain Research (Amsterdam). 115(1):111-128, 1976.

The mechanism underlying the depressant actions of narcotic analgesics on neuronal discharge activity and the interaction of these drugs with putative neurotransmitters were investigated in cats. In the majority of spinal neurones microelectrophoretically applied morphine and levorphanol reversibly depressed spontaneous activity, stimulus evoked activity and activity induced by L-glutamate or acetylcholine. The depressant effects of opiates were antagonized by naloxone and generally were not associated with hyperpolarization of the cell. Dextrorphan displayed no depressant actions, indicating that stereospecific receptors mediate the depressant effects of opiates. The hyperpolarizing effects of glycine was not influenced by opiates in dosage levels sufficient to suppress depolarization induced by glutamate or acetylcholine. Intravenous administration of morphine or Fentanyl also depressed spontaneous activity and evoked neuronal activity. The results are discussed with respect to a stereospecific action of opiates at a postsynaptic receptor site in the spinal cord. 40 references. (Author abstract modified)

001430 Zsilla, G.; Cheney, D. L.; Racagni, G.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 Correlation between analgesia and the decrease of acetylcholine turnover rate in cortex and hippocampus elicited by morphine, meperidine, viminal R2 and azidomorphine. Journal of Pharmacology and Experimental Therapeutics. 199(3):662-668, 1976.

The role of acetylcholine (ACh) in the mediation of central analgesic action was studied by measuring the effects of morphine, meperidine, viminal R-2 and azidomorphine on the turnover rate of ACh (TRACH) in various areas of the rat brain. All four analgesics decreased TRACH in cortex and hippocampus but not in striatum. Viminal S2, a nonanalgesic stereoisomer of viminal R2, failed to decrease the TRACH in cortex and hippocampus. Naltrexone, an opiate antagonist, antagonized the decrease in cortical and hippocampal TRACH induced by the analgesics without having a direct effect on TRACH in these structures. It is suggested that opiate receptors are not exclusively involved in the regulation of TRACH but that certain cholinergic pathways participate in the mediation of analgesia. 41 references. (Author abstract modified)

001431 Zsilla, G.; Cheney, D. L.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 Regional changes in the rate of turnover of acetylcholine in rat brain following diazepam or muscimol. Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(3):251-255, 1976.

Muscimol (8.8umol/kg i.v.) and diazepam (7.04umol/kg i.p.) decreased the rate of turnover of acetylcholine in midbrain and cortex of rat brain but failed to change acetylcholine turnover in striatum and hippocampus. The similarity in the profile of the action of diazepam and muscimol on

acetylcholine turnover in various brain structures adds support to the view that gamma-aminobutyric acid (GABA) participates in mediating the actions of diazepam. Since the striatum contains an abundance of GABA neurones and intrinsic cholinergic neurones, it is inferred that the metabolism of acetylcholine, and presumably the activity of striatal cholinergic neurones are not regulated by the activation of GABA receptors. Similar considerations apply to the cholinergic pathway projecting from the septum to the hippocampus. 22 references. (Author abstract)

001432 Zsilla, G.; Cheney, D. L.; Costa, E. Department of Pharmacology, Semmelweis University of Medicine, Budapest, Hungary **Acetylcholine turnover rate in specific brain nuclei: effects of narcotic analgesics.** In: Proceedings of a Symposium: Factors affecting the action of narcotics. NIMH, St. Elizabeths Hospital, 1976. 21 p.

The correlation between opiate analgesia and the modulation of the turnover rate of acetylcholine (TR-ACH) in brain areas containing different densities of opiate receptors was investigated in rats. Morphine, meperidine, azidomorphine and viminal R-2, four narcotic analgesics with different chemical structures, inhibit the TR-ACH in cortex and hippocampus but not in striatum. Morphine inhibits TR-ACH in nucleus accumbens but not in other brain nuclei. Naltrexone, an opiate antagonist decreases or antagonizes the reduction in TR-ACH but when given alone, naltrexone does not change TR-ACH in striatum, cortex or hippocampus. Naltrexone also reverses the reduction of TR-ACH. The action of opiate analgesics on the TR-ACH of a given brain structure does not appear to depend exclusively on the density of opiate receptors present. It is suggested that the decrease in hippocampal TR-ACH reflects primarily a regulatory action of the cholinergic cell bodies on septum by opiate receptors. It is also suggested, however, that opiate receptors are not universal modulators of cholinergic neurons although they may have a regulatory influence on cholinergic neurons as well as other kinds of neurons. The conclusion that morphine does not act primarily on cholinergic neurons is upheld. 43 references.

04 MECHANISM OF ACTION: BEHAVIORAL

001433 Adams, P. M.; Barratt, E. S. Behavioral Science Laboratory, Department of Psychiatry, University of Texas Medical Branch, Galveston, TX 77550 **Effect of chronic pentobarbital treatment on the sleep patterns of squirrel monkeys.** Psychopharmacology (Berlin). 48(2):205-207, 1976.

A study was carried out in squirrel monkeys to determine the effects of prolonged (60 days) sodium pentobarbital administration on sleep patterns and to determine the rate of recovery from altered sleep patterns. Repeated pentobarbital treatment significantly reduced awake time and slow-wave sleep, while it elevated the time spent in drowsy and light sleep. The recovery phase indicated a brief recovery of rapid eye movement sleep while the other stages failed to return to baseline levels. The cyclical nature of the changes observed with chronic pentobarbital suggest the importance of circadian fluctuations in the study of chronic drug treatment and the sleep/wakefulness process. 9 references. (Author abstract modified)

001434 Agmo, Anders. Department of Zoophysiology, University of Uppsala, Box 560, S-75122 Uppsala, Sweden **Cholinergic mechanisms and sexual behavior in the male rabbit.** Psychopharmacology (Berlin). 51(1):43-45, 1976.

The effects of cholinolytic agents and cholinomimetic agents on sexual behavior were investigated in castrated male rabbits treated with testosterone. Scopolamine and methylscopolamine inhibited sexual activity in doses of 0.1mg/kg but not in doses of 0.02mg/kg. Pilocarpine completely inhibited sexual activity at doses of 2mg/kg, 10mg/kg and 50mg/kg. A subeffective dose of methylscopolamine completely antagonized the effects of 2mg/kg pilocarpine; partially antagonized the effects of 10mg/kg pilocarpine; and had no effect on the 50mg/kg dose. Scopolamine completely antagonized the effects of 2mg/kg pilocarpine and 10mg/kg pilocarpine, but had no effect on the 50mg/kg dose. It is suggested that the peripheral effects of both the receptor blocking agents and the receptor stimulating agents are most important for the effects on sexual behavior, although a central site of action of pilocarpine cannot be ruled out. 6 references. (Author abstract modified)

001435 Anisman, Hymie; Kokkinidis, Larry; Glazier, Steve; Remington, Gary. Carleton University, Ottawa, Ontario K1S 5B6, Canada **Differentiation of response biases elicited by scopolamine and d-amphetamine: effects on habituation.** Behavioral Biology. 18(3):401-417, 1976.

Behavioral changes induced by scopolamine and d-amphetamine in mice in a transfer paradigm were investigated and the differences in the nature of the nonassociative processes involved are discussed. The effects of the drugs were evaluated in a water approach task following stimulus preexposure and in the habituation of locomotor activity. Stimulus preexposure reduced the response rate of approaching a water source upon reexposure to the stimulus complex. Strain differences between mice were observed in the effects of the preexposure treatment, although the approach rate was directly related to the duration of preexposure in both strains. Although scopolamine and d-amphetamine differentially affected locomotor activity in the two strains, both drugs eliminated the effects of preexposure and attenuated the course of habituation of locomotor activity equally in all the mice. In addition, d-amphetamine produced carryover effects in terms of increased locomotor activity. Results were interpreted in terms of the immediate and carryover effects elicited by the drugs, i.e., response disinhibition/dishabituation in the case of scopolamine and genuine response excitation with d-amphetamine. Alternative explanations such as proactive drug effects, effects on memory consolidation, drug dissociation, or drug x deprivation interaction did not account for the observed findings. 27 references. (Author abstract)

001436 Atkinson, J.; Enslin, M. Physiology and Pharmacology Laboratories, Nestle Products Technical Assistance Co., CH-1350 Orbe, Switzerland **Self-administration of caffeine by the rat.** Arzneimittel-Forschung (Aulendorf). 26(11):2059-2060, 2061, 1976.

The question of whether rats will administer caffeine to themselves was studied in female Sprague-Dawley individuals. About 2 weeks before each experiment, cannulae were implanted in the right jugular vein. Rats were placed in a box with a lever, the pressing of which enabled them to self-inject 1.5 to 5mg/kg caffeine. Some of the rats were pretreated with caffeine before being given the chance to self-inject, while others were not pretreated. Some of the rats self-administered caffeine and others did not; thus the drug abuse potential of this drug appears to be low. 11 references.

001437 Babbini, M.; Gaiardi, M.; Bartoletti, M. Institute of Pharmacology, University of Bologna, Bologna, Italy **Some behavioral effects of prethamide compared with those of its two components.** Pharmacology (Basel). 14(5):455-463, 1976.

The effects of the two components of prethcamide (namely crotetamide and cropropamide) upon various behaviors in rats were compared with those of prethcamide itself to see if both were active or not and the kind of joint action shown when they were given in combination. Both crotetamide and cropropamide increase the motor activity of rats, reduce the rate of lever pressing in fixed ratio (FR) and variable interval (VI) food reinforced schedules and increase the latency times in a multiple continuous reinforcement (CRF) discrimination schedule. When given in combination the drugs show additive effects upon locomotor activity and FR or VI behaviors but they potentiate each other as regards the effects upon latency times in the multiple schedule. On the other hand, a clear antagonism between the two drugs has been found in the acute toxicity test. 18 references. (Author abstract)

001438 Baker, W. W.; Zivanovic, D.; Malseed, R. T. Division of Neuropharmacology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA Tremorogenic effects of intracaudate d-amphetamine and their suppression by dopamine. *Archives internationales de Pharmacodynamie et de Therapie* (Ghent). 223(2):271-281, 1976.

The effects of intracaudate (IC) injections of dextroamphetamine, several dextroamphetamine analogs, and several pharmacologically related adrenergic agents were examined in cats in order to determine how specific the local effects of dextroamphetamine in the caudate are. Pronounced tremors were produced following IC injections of either d-amphetamine, dl-methamphetamine, l-amphetamine, or 3-methoxytyramine. Other chemically and pharmacologically related phenylethylamines, including dopamine (DA) were not tremorogenic even at substantially higher doses. Significant qualitative differences were found between the I.C. effects of d-amphetamine and DA. d-Amphetamine further increased the intensity of ongoing tremors induced by physostigmine, whereas DA readily inhibited the latter. When superimposed, I.C. DA was equally effective in suppressing d-amphetamine tremor activity. The results emphasize the selective tremorogenic actions of d-amphetamine and call attention to the contrasting stabilizing role of DA. It is suggested that two types of adrenergic receptor sites are operative in the caudate in neuroregulation of involuntary movements. 26 references. (Author abstract modified)

001439 Ballhause, H.; Kahling, J. Biologische Forschung, Birkendorfer Str. 65, D-7950 Biberach an der Riss, Germany /A device for the evaluation of motor incoordination in rats./ Ein Apparat zur Messung motorischer Funktionsstörungen bei Ratten. *Psychopharmacology* (Berlin). 50(3):281-283, 1976.

A runway apparatus for rats developed for measuring motor incoordination and running time is described. Animals were trained to run along an elevated narrow pathway. Frequency and severity of slipping off and running time were automatically counted. Rats were given diazepam, phenobarbital or chlorpromazine orally and tested 1 h later. Diazepam caused slipping off in a dose dependent manner. Phenobarbital had a similar effect. Chlorpromazine caused other signs of motor deficit. 5 references. (Author abstract)

001440 Banerjee, Utpal; Das, Pronati. Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia Variable temporal gradients of retrograde amnesia: contingency on tasks and species. *Behavioral Biology*. 18(3):447-453, 1976.

Retrograde amnesia gradients contingent on task, treatment and species variables were investigated by training rats to

acquire active avoidance and passive avoidance and associative escape learning within 10 min. Amnesic treatments with electroconvulsive shock, pentylenetetrazol, or pentobarbitone followed at varying intervals from the onset of training. Tested for retention 24 hr later, they showed task variable temporal gradients of retrograde amnesia even with the same treatment. ECS amnesia had the shortest gradients, ranging from 3 to 15 min, the pentobarbitone gradient was up to 15 min in the escape learning, whereas pentylenetetrazol produced amnesia with longer gradients of 4 to over 30 min. Mice used in the escape learning task showed longer gradients than rats with all three treatments. 13 references. (Author abstract modified)

001441 Baugh, R.; Calvert, R. T. Department of Pharmacy, Manchester University, Manchester, England The effect of ethanol and diphenhydramine on histamine antagonism and mental performance tests in man. *Journal of Pharmacy and Pharmacology* (London). 28(Supplement):41P, 1976.

The effects of the diphenhydramine alone or in combination with alcohol on histamine response and on mental performance in 12 male volunteers were studied. Each volunteer received either 500mg/kg alcohol or 75mg/kg diphenhydramine (DPH) or both at weekly intervals in a double-blind trial. The tests of mental performance were digit symbol substitution, serial seven subtraction, and movement of a loop over a twisted wire. The digit symbol substitution showed nonsignificant differences at early time points, while on the wire and loop test, performance was improved with ethanol and depressed with DPH. Performance with alcohol and alcohol + DPH on this test did not differ significantly. DPH impaired performance on the serial seven subtraction test, and this impairment was increased by ethanol. Ethanol had no effect on the histamine challenge test and did not affect the effectiveness of DPH. It is suggested that the interaction between DPH and ethanol is at its site of sedative action, and results of the serial seven test suggest that it may be synergistic in nature. 3 references.

001442 Beckmann, Horst-Ernst; Chaplain, Ronald A. Dept. of Physiology, University of Mainz, 65 Mainz, Germany Effects of fructose-1,6-diphosphate administration on learning efficiency and time sense of the honey bee, *Apis mellifica carnica*. *Brain Research* (Amsterdam). 114(3):461-470, 1976.

Honey bees of the species *Apis mellifica carnica* were trained in the schedule devised by von Frisch (modified by Beckman), and the effects of fructose-1,6-diphosphate (F-1,6-P2) administration on learning efficiency and time sense were measured. No change in general activity or harvesting motivation appears to be induced by F-1,6-P2. Ingestion of other metabolites proved either ineffective, as in the case of fructose-6-phosphate or 5'-adenosine monophosphate, or, reduced performance as in the case of citrate plus 3-phosphoglycerate. To test the effect of F-1,6-P2 on the time sense (circadian rhythm), bees were trained on three successive days to visit a feeding place at a specific time of day. The control bees which ingested only glucose on the evening of the 3rd day returned at their entrained 24 hour interval on the 4th day. In contrast, the maximum frequency of appearance of bees fed on F-1,6-P2 was advanced by 1 hour, with minor appearance peaks at earlier hours of the day. 31 references. (Author abstract modified)

001443 Bermond, Bob; Van de Poll, Nanne E.; Van Dis, Huib. Netherlands Central Institute for Brain Research, IJdijk 28, ND-1006 Amsterdam, The Netherlands Reserpine induction of mouse killing in nonkiller rats. *Bulletin of the Psychonomic Society*. 8(1):49-50, 1976.

To investigate reserpine induction of mousekilling in non-killer rats, 75 male Wistar rats were divided into two groups, 38 animals receiving 3mg/kg reserpine and the other 37 receiving saline. Of the reserpine treated animals, 50% showed mousekilling, whereas none of the other animals did so. Mouse kill responses were already exhibited within 32 hr after treatment, while the animals were still heavily sedated. Findings suggest support for an inhibitory role of both noradrenaline and serotonin in regulation of the mouse kill response since reserpine causes depletion of noradrenaline and serotonin stores. Reserpine also results in increased acetylcholine in the hypothalamus and other brain parts, and these data, coupled with those from studies on cholinergic regulation of mousekilling and clinical use of reserpine with severely depressed patients, give further support for development of an animal model of human depression. 21 references. (Author abstract modified)

001444 Beyer, C.; Morali, G.; Naftolin, F.; Larsson, K.; Perez-Palacios, G. Departamento de Biología de la Reproducción, Universidad Autónoma Metropolitana - Iztapalapa, Mexico Effect of some antiestrogens and aromatase inhibitors on androgen induced sexual behavior in castrated male rats. *Hormones and Behavior*. 7(3):353-363, 1976.

Summaries of two studies testing the effect of antiestrogens (MER-25, ICI-46474, and cis-clomiphene) and aromatase inhibitors (5-alpha-androstane-3-one, metopirone, and aminoglutethimide) are presented on androgen induced copulatory behavior in sexually inexperienced castrated male rats. Daily injections of 1mg testosterone (T) for 21 days induced sexual activity in most subjects. Daily pretreatment with MER-25 or cis-clomiphene at three dose levels did not block the behavioral response to T. At the high dose level, ICI-46474 elicited a significant depressory effect on the sexual behavior of the T treated castrated rats. A single injection of 6mg testosterone propionate (TP) induced mounting behavior in 56% of the tested rats within 120 hours. Treatment with metopirone or 5-alpha-androstane-3-one (injections every 12 hours for 96 hours) did not inhibit the response to TP. By contrast, aminoglutethimide abolished the behavioral response to androgen. It is recommended that further work be done to explain the mechanism through which this last effect takes place. 27 references. (Author abstract modified)

001445 Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, College of Pharmacy, Univ. of Illinois at the Medical Center, P. O. Box 6998, Chicago, IL 60680 Effect of some cannabinoids on naloxone-precipitated abstinence in morphine-dependent mice. *Psychopharmacology (Berlin)*. 49(3):267-270, 1976.

The effects of delta9-tetrahydrocannabinol (delta9-THC), delta8-tetrahydrocannabinol (delta8-THC), cannabinol, cannabidiol, and 11-hydroxy-delta8-tetrahydrocannabinol, a metabolite of delta8-THC, on naloxone precipitated withdrawal in morphine dependent mice was studied. Mice were rendered morphine dependent by the subcutaneous implantation of a pellet containing 75mg of morphine base; 72 hours after the implantation, the animals were injected intraperitoneally either with vehicle or with various doses of delta9-THC, delta8-THC, cannabidiol, cannabinol, or 11-hydroxy-delta8-THC. Thirty minutes after injection of the cannabinoids, the antagonist, naloxone HCl, was administered to induce the stereotyped withdrawal jumping syndrome. The dose of naloxone needed to induce withdrawal jumping in 50% of the animals was determined for each dose of the cannabinoids. All of the cannabinoids inhibited the naloxone

precipitated morphine abstinence as evidenced by an increase in the naloxone ED50. Two additional signs of morphine abstinence, defecation and rearing behavior, were also suppressed by the cannabinoids. The relative effectiveness of the cannabinoids in inhibiting morphine abstinence appeared in the following diminishing order: delta9-THC, delta8-THC, 11-hydroxy-delta8-THC, cannabidiol. These data suggest that cannabinoids may be useful in facilitating narcotic detoxification. 25 references. (Author abstract modified)

001446 Bhattacharya, S. K.; Pandey, V. B.; Ray, A. B.; Dasgupta, B. Department of Pharmacology and Medicinal Chemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, India Neuropsychopharmacological studies with (-)-tetrahydrocannabinol. *Arzneimittel-Forschung (Aulendorf)*. 26(12):2187, 1976.

The neuropsychopharmacological actions of levotetrahydrocannabinol were studied in rats and mice. The drug produced marked sedation, ptosis and diminished activity in albino rats and mice. With increasing doses, the drug produced catalepsy. Other effects noted were: 1) reduction of spontaneous motor activity in mice; 2) marked potentiation of hexobarbital sleeping time; 3) significant antagonism of amphetamine toxicity in aggregated rats; 4) complete inhibition of LSD induced piloerection and tremors in rats and mescaline induced scratching response in mice; 5) slight inhibition of the ability of trained mice to remain on a rotating rod; 6) selective blockade of the avoidance response to a conditioned stimulus without any effect on the escape response to an unconditioned stimulus in trained rats; 7) potentiation of the analgesic activity of a subanalgesic dose of morphine without having analgesic activity of its own; and 8) potentiation of the anticonvulsant activity of a subeffective dose of phenytoin while having no anticonvulsant effect of its own. It is suggested that levotetrahydrocannabinol has a chlorpromazine like profile of antipsychotic (neuroleptic) activity. 13 references.

001447 Blasig, J.; Gramsch, C.; Laschka, E.; Herz, A. Department of Neuropsychopharmacology, Max-Planck-Institute of Psychiatry, Kraepelinstrasse 10, D-8000 Munich 40, Germany The role of dopamine in withdrawal jumping in morphine dependent rats. *Arzneimittel-Forschung (Aulendorf)*. 26(6):1104-1106, 1976.

The role of brain dopamine in withdrawal jumping was investigated in rats using three different approaches. The rats had received 6 pellets s.c. within 7 days, each pellet containing 75 mg of morphine base. Withdrawal was precipitated by 1mg/kg naloxone given 3 days after the last pellet. Shortly before withdrawal, the rats were treated with one of five dopamine agonists: apomorphine, 1,3-dimethyl-5-aminoadamantane, 2-bromo-alpha-ergocryptine, piribedil, or 1-isopropyl-4,4-diphenylpiperidine hydrochloride. All five substances induced a significant frequency of withdrawal jumping. Pimocidol inhibited the jumping facilitating effect of piribedil, but did not inhibit the naloxone induced jumping. After naloxone, striatal dopamine was increased by 30%, turnover of 3,4-dihydroxyphenylacetic acid and homovanillic acid in the striatum was decreased by 25% and 20%, respectively, following probenecid, and the level of 3-methoxytyramine decreased 40%. These data suggest a reduced neuronal dopamine release or reduced dopamine catabolism resulting in an increased amount of dopamine at the receptor site. Unilateral inactivation of one caudate nucleus by intracerebral injection of KCl caused contralateral circling following naloxone. Halperidol slightly increased the naloxone induced contralateral circling, while apomorphine changed the circling direction from contra-

lateral to ipsilateral. These findings point to striatal dopamine deficiency during withdrawal. 24 references.

001448 Boissier, J. R.; Dumont, C.; Oberlander, C.; Peterfalvi, M. Roussel-Uclaf, B.P. 9, F-93230 Romainville, France. A comparison of circling behaviour induced in nigro-striatal lesioned rats after peripheral administration of indole derivatives. *British Journal of Pharmacology* (London). 58(3):452P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed a number of compounds related to tryptamine and three piperidyl indole derivatives for their effects on the circling behavior in nigro-striatal lesioned rats. Tryptamine and its derivatives were inactive as well as methysergide while lysergic acid diethylamide (LSD) caused ipsilateral circling at high dose, in striatal rats. Piperidyl indole and the 5-hydroxy derivative had no effect, but the 5-methyl derivative induced a long-lasting contralateral turning behavior. Following scopolamine administration, LSD induced ipsilateral turning was potentiated, and a strong contralateral rotating behavior with piperidyl indole was revealed. In nigral lesioned rats, the tested compounds were inactive, except LSD which induced strong contralateral turning, and 5-methylpiperidyl indole which provoked a biphasic response only at the highest dose. The results suggest that there is not clear evidence for a role of tryptaminergic pathways in the mechanism of circling, and that rotations may not solely originate from a classical dopamine receptor stimulating action. 4 references.

001449 Boren, James L.; Gallup, Gordon G., Jr. no address. Amphetamine attenuation of tonic immobility in chickens. *Physiological Psychology*. 4(4):429-432, 1976.

Contrary to the contention that the duration of tonic immobility may reflect monotonic changes in arousal, different doses of d-amphetamine were shown to differentially antagonize the reaction in chickens. Not only were response durations abbreviated, but amphetamine was also found to diminish overall susceptibility to immobility. The possibility of an amphetamine induced increase in general activity as an alternative account of immobility attenuation was ruled out in the second experiment. In a third experiment, it was shown that the effect of amphetamine on response duration could be abolished by pretreatment with para-chlorophenylalanine. 18 references. (Author abstract)

001450 Breuker, E.; Dingledine, R.; Iversen, L. L. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Cambridge, England. Evidence for naloxone and opiates as GABA antagonists. *British Journal of Pharmacology* (London). 58(3):458P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the behavioral effects of naloxone and opiates as a result of GABA antagonism in mice. Naloxone caused convulsions while pretreatment of mice with a subconvulsant dose of naloxone significantly reduced the ED50 for bicuculline convulsions while not affecting the dose response for strychnine. Diazepam pretreatment significantly increased the ED50 of both bicuculline and naloxone without affecting strychnine induced convulsions. In vitro experiments with human brain homogenates and single rat neurons showed the ability of bicuculline, naloxone, morphine, levorphanol, and dextrorphan to displace tritiated GABA from receptor sites. It is posited that the behavioral excitation seen after administering large amounts of some opiates or opiate antagonists may reflect functional receptor blockade of GABA inhibitory systems. 2 references.

001451 Brewster, J. M.; Siegel, R. K.; Johnson, C. A.; Jarvik, M. E. Department of Pharmacology, University of California, Los Angeles, CA 90024. Observational determination of dose-response curves in hallucinogen-treated monkeys. *International Pharmacopsychiatry* (Basel). 11(2):102-108, 1976.

An objective behavioral profile that was previously shown to distinguish the effects of hallucinogens from those of other classes of drugs was used to further study hallucinogenic behaviors. Saline, d-amphetamine sulfate, and five doses of dimethyltryptamine (DMT) were administered to solitary adult rhesus monkeys in a dark environment. Scores in the following categories systematically increased with ascending doses of DMT: exploration, locomotion, stereotypy, spasm, tracking, and duration of inappropriate behavior. Some behaviors sensitive to hallucinogens occurred with greater frequency in the dark than in a previous study conducted in the light. Behaviors such as tracking and fear grimaces emerged in the absence of stimuli in the dark. It was concluded that hallucinogen induced changes were produced in perceptual motor systems. 9 references. (Author abstract modified)

001452 Brown, Randolph F.; Houpt, Katherine Albro; Schryver, Herbert F. New York State College of Veterinary Medicine, Cornell University, Ithaca, NY 14853. Stimulation of food intake in horses by diazepam and promazine. *Pharmacology Biochemistry and Behavior*. 5(4):495-497, 1976.

The effects of diazepam and of promazine on food intake were examined in horses. In adult horses, diazepam increased 1 hr intake up to 75% above control levels. Intake was stimulated when the diet was a high grain, calorically dense one and also when the diet was a high fiber, calorically dilute one. Two young rapidly growing weanling horses showed an even more pronounced stimulation of intake. Promazine also stimulated intake in adult horses, but not as markedly as did diazepam. It is concluded that both drugs have a stimulatory effect upon short-term intake in horses. 7 references. (Author abstract modified)

001453 Byrd, L. D. Division of Primate Behavior, Yerkes Regional Primate Research Center, Emory University, Atlanta, GA 30322. Effects of morphine alone and in combination with naloxone or d-amphetamine on shock-maintained behavior in the squirrel monkey. *Psychopharmacology* (Berlin). 49(3):225-234, 1976.

The behavioral effects of morphine alone and in combination with naloxone or d-amphetamine when responding in the squirrel monkey was maintained under a schedule of response produced electric shock were studied. The administration of 1.0mg/kg to 3.0mg/kg of morphine prior to daily sessions decreased response rates, but doses of 0.03mg/kg to 0.3mg/kg had little systematic effect on rates. When naloxone was administered concomitantly with morphine prior to a session, 0.01mg/kg naloxone required a three fold increase in the dose of morphine necessary to obtain decreased response rates, 0.1mg/kg naloxone required a 30 fold increase in morphine. Moreover, the administration of naloxone with morphine resulted in increased rates of responding at certain combinations of doses of the two drugs. The administration of d-amphetamine alone increased mean response rates under the fixed interval (FI) schedule; when combined with 0.03mg/kg to 0.3mg/kg morphine the increases in responding were greater than obtained with d-amphetamine alone. These results show that naloxone, but not d-amphetamine, can antagonize the response rate decreasing effect of morphine when responding in the squirrel monkey is maintained by response produced electric shock. 38 references. (Author abstract modified)

001454 Carney, John M.; Llewellyn, Mark E.; Woods, James H. Department of Pharmacology, MCV Station 726, Medical College of Virginia, Richmond, VA 23298 **Variable interval responding maintained by intravenous codeine and ethanol injections in the Rhesus monkey.** *Pharmacology Biochemistry and Behavior.* 5(5):577-582, 1976.

A study was carried out in Rhesus monkeys to determine: 1) whether the dose related negative acceleration of responding observed for ethanol and codeine reinforcement under fixed rate schedules would also occur under a variable interval schedule of reinforcement; 2) the relationship between the reinforcer dose of codeine or ethanol and the degree of negative acceleration observed; and 3) the effects of changing the magnitude of the codeine reinforcer dose midway through the session. Both drugs were effective in the initiation of variable interval responding; responding was maintained over a range of doses. Rates of responding were bitonic functions of the reinforcer dose for both codeine and ethanol; maximum rates were obtained at intermediate doses and lower rates occurred at both extremes of the dose range. Both drugs showed within session decreases in responding across the range of doses. Codeine reinforced responding declined in rate without a similar change in the frequency of drug injection. In contrast, both ethanol reinforced responding and the frequency of ethanol injections declined within each session across a range of doses. Changes in the dose of codeine halfway through the one hour session produced changes in codeine responding. It is concluded that the progressive decline in codeine reinforced responding is not the result of a generalized disruption of responding. 19 references. (Author abstract modified)

001455 Cazala, Pierre. Laboratoire de Psychophysiologie, Université de Bordeaux I, Avenue des Facultés, 33405 Talence, France **Effects of d- and l-amphetamine on dorsal and ventral hypothalamic self-stimulation in three inbred strains of mice.** *Pharmacology Biochemistry and Behavior.* 5(5):505-510, 1976.

The effects of intraperitoneal injections of increasing doses of dextroamphetamine and levoamphetamine on self-stimulation behavior in the dorsal hypothalamus and ventral hypothalamus were studied in BALB/c Orl, DBA/2 Orl, and C57BL/6 Orl inbred mice. Both isomers improved and disrupted self-stimulation as a function of the doses injected. The improvements obtained with dextroamphetamine were higher than those obtained with levoamphetamine, while levoamphetamine generally provoked the largest disruptions. The BALB/c mice were most sensitive to improvements in self-stimulation induced by dextroamphetamine and the C57BL/6 mice were the least sensitive. The dorsal hypothalamic self-stimulation system was more sensitive to dextroamphetamine than the ventral system, but both systems reacted identically to levoamphetamine. The differential effects observed are discussed in relation to neurochemical data concerning the central catecholaminergic mechanisms. 40 references. (Author abstract modified)

001456 Cerny, Veronica A. Department of Animal Biology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19174 **The influence of hypothalamically administered reserpine on the sexual behavior of the female cat.** *Psychopharmacology (Berlin).* 50(3):269-274, 1976.

Ovariectomized cats with intracerebral implants of reserpine, a monoamine depletor, were tested for sexual behavior by introducing them to sexually vigorous males and by artificial stimulation. Approximately a third of the animals mated in response to reserpine and another third exhibited some com-

ponents of sexual behavior. The behavior exhibited by these animals had none of the frenzy of normal estrous behavior. Some components of the normal pattern were missing while all others were curtailed in duration and vigor. These animals responded with normal sexual behavior to intracerebrally and systemically administered estrogen. It is suggested that the unusual sexual behavior in response to reserpine was due to the release of these behavioral patterns from a monoamine system, inhibitory to sexual behavior. 52 references. (Author abstract)

001457 Chen, C. S.; Gates, G. R.; Reynoldson, J. A. Department of Psychology, Monash University, Clayton, Victoria, Australia **Effect of morphine and naloxone on priming-induced audiogenic seizures in BALB/c mice.** *British Journal of Pharmacology (London).* 58(4):517-520, 1976.

The effects of morphine and naloxone on priming induced audiogenic seizures was studied in normally seizure resistant BALB/c mice. Morphine reduced the incidence and prolonged the latency of the seizures in a dose dependent manner. This effect was reversed by naloxone, although naloxone was ineffective in altering the incidence of any seizure component alone. It is suggested that the effects of morphine on the seizures is mediated through a specific naloxone sensitive receptor and that the priming induced seizure model may be useful in the study of tolerance and physical dependence. 18 references. (Author abstract modified)

001458 Clavier, Ronald M.; Fibiger, Hans C.; Phillips, Anthony G. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, B.C. V6T 1W5, Canada **Evidence that self-stimulation of the region of the locus coeruleus in rats does not depend upon noradrenergic projections to telencephalon.** *Brain Research (Amsterdam).* 113(1):71-81, 1976.

The hypothesis that the role of the locus coeruleus (LC) in brainstem intracranial self-stimulation (ICSS) is related to the widespread noradrenergic innervation by LC neurons of diencephalic regions and telencephalic regions was investigated. Rats with ICSS electrodes in the LC and adjacent pontine tegmental structures received stereotactically placed bilateral injections of 6-hydroxydopamine into the mesencephalic trajectory of the dorsal tegmental noradrenergic bundle. The consequent depletions of norepinephrine in the cerebral cortices and hippocampi did not result in significant changes in ICSS. Thus, diencephalic and telencephalic noradrenergic projections of the LC do not appear to be critical for the occurrence of ICSS from that nucleus or its surrounding region. Nor do these projections appear to be crucially involved in the enhancement of this ICSS by D-amphetamine. Rats showed twofold increases in responding following injections of D-amphetamine sulfate both before and after the lesions of the dorsal tegmental bundle. It is suggested that the ascending projections of the locus coeruleus are not critically involved in ICSS of the dorsal pontine tegmentum. 31 references. (Author abstract modified)

001459 Clineschmidt, B. V.; Hanson, H. M.; McGuffin, J. C.; Lotti, V. J.; Scriabine, A.; Stone, C. A. Merck Institute for Therapeutic Research, West Point, PA 19486 **Appetite stimulant activity of 3-carboxy-10,11-dihydroxyproheptadine.** *Archives internationales de Pharmacodynamie et de Therapie (Ghent).* 223(2):287-300, 1976.

The orexigenic and ancillary pharmacologic properties of 3-carboxy-10,11-dihydroxyproheptadine (CDC) were compared to those of cyproheptadine, using cats, guinea pigs, mice, and

rats. The threshold dose of CDC for increasing food intake in the rat is similar to that of cyproheptadine, but CEC has a broader effective dose range. Using an increase in food consumption of 20% or more as the criterion of a positive response, the dose effective in 50% of the animals was 0.35mg/kg p.o. for both CDC and cyproheptadine. Both drugs possess a long duration of appetite stimulating action, exceeding 18 hr. The anticholinergic, antiserotonin, and locomotor depressant effects of CDC are considerably less than those of cyproheptadine but CDC is about twice as potent in antihistaminic activity. It is suggested that CDC is a more selective agent for the therapy of anorexia. 25 references. (Author abstract modified)

001460 Colpaert, F. C.; Kuyps, J. J. M. D.; Niemegeers, C. J. E.; Janssen, P. A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340, Beerse, Belgium **Discriminative stimulus properties of a low dl-amphetamine dose.** Archives internationales de Pharmacodynamie et de Therapie (Ghent). 223(1):34-42, 1976.

To test the discriminative stimulus properties of low dl-amphetamine doses, rats (n=10) were trained to discriminate 0.16mg/kg dl-amphetamine from saline. Over the dose range .08mg/kg to .63mg/kg, cue detection was found to be dose dependent. However, 5mg/kg of dl-amphetamine was not generalized with the standard treatment. Further generalization experiments indicated that a low dose of hydroxyamphetamine produces a discriminative stimulus similar to that of a low dose of dl-amphetamine. Apomorphine, chloridazepoxide, desipramine, fentanyl, haloperidol, and isopropamide were not generalized with dl-amphetamine. Haloperidol (.04mg/kg to .16mg/kg) blocked the perception of .16mg/kg dl-amphetamine in a dose related way. It is concluded that the discriminative stimulus properties of low dl-amphetamine doses differ qualitatively from those of a high dose. The discriminative stimulus produced by .16mg/kg of dl-amphetamine presumably originated peripherally, whereas that produced by high doses of the drug reportedly is of central origin. 29 references. (Author abstract modified)

001461 Colpaert, F. C.; Kuyps, J. J. M. D.; Niemegeers, C. J. E.; Janssen, P. A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Discriminative stimulus properties of fentanyl and morphine: tolerance and dependence.** Pharmacology Biochemistry and Behavior. 5(4):401-408, 1976.

To determine whether the discriminative stimulus properties of narcotic analgesics are subject to tolerance, rats were trained to discriminate fentanyl from saline, after which stimulus generalization was determined using equivalent doses of fentanyl and morphine. Neither tolerance to the discriminative stimulus properties of fentanyl nor cross-tolerance with morphine were evident; however, marked tolerance to the analgesic effects of the drugs occurred. Withdrawal symptoms were not induced by intravenous injection of naloxone or by drug withdrawal, indicating that the animals used in the discriminative stimulus testing had not developed narcotic dependence. It is concluded that the discriminative stimulus properties of narcotic analgesics are not subject to tolerance. 35 references. (Author abstract modified)

001462 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, Beerse, Belgium. **Cocaine cue in rats as it relates to subjective drug effects: a preliminary report.** European Journal of Pharmacology (Amsterdam). 40(1):195-199, 1976.

Cocaine cue in rats as it relates to subjective drug effects was studied. Rats trained to discriminate cocaine solution from saline using a food reinforced two lever operant method revealed that the cocaine cue is a dose related phenomenon. Neuroleptic drugs were generally found to be ineffective as possible antagonists to the cocaine cue and no antagonistic effect was obtained with dibenamine, propranolol, cyproheptadine and methysergide, while the effect of pimoide and haloperidol is slight. Both amphetamine and apomorphine were generalized with cocaine in the five rats tested for this effect. The results suggest that increased central dopaminergic activity is associated with the cuing properties of cocaine; however, the relative ineffectiveness of haloperidol and pimoide as antagonists discourage a simple dopaminergic interpretation. The present results indicate that the possibility of the cocaine cue as a valuable model for therapy resistant subjective drug effects exists. 12 references. (Author abstract modified)

001463 Curzon, G.; Marsden, C. A. Department of Neurochemistry, Institute of Neurology, Queen Square, London WC1 3BG, England **Effects of p-chlorophenylalanine and alpha-methyltryptophan on rat social behaviour.** British Journal of Pharmacology (London). 58(3):455P-456P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of p-chlorophenylalanine (PCPA) and alpha-methyltryptophan (AMTP) on rat social behavior. Both drugs reduced food intake at 24 hrs, but it was normal at 72 hrs. PCPA significantly reduced 5-hydroxytryptamine (5-HT) levels in the brain, increased locomotor activity, and increased interactions between rats including sniffing, biting, fighting, and mounting behavior. In contrast, AMTP increased brain 5-HT levels and had no significant effect on any of the social behavior components or net locomotor activity. However, self-grooming and burrowing increased at 24 hrs. The results suggest that when AMTP is administered, the formation of alpha-methyl-5-HT opposes the behavioral effects of decreased 5-HT synthesis. 5 references.

001464 Dalhouse, A. Derick. Ohio State University, Laboratory of Comparative and Physiological Psychology, Columbus, OH 43212 **Social cohesiveness, hypersexuality and irritability induced by p-CPA in the rat.** Physiology and Behavior. 17(4):679-686, 1976.

The relationship between the social cohesiveness, hypersexuality, and irritability induced by para-chlorophenylalanine (p-CPA) in the rat, and that following ablations of the septum, was investigated. Lesions of the septal forebrain were found to produce behavioral changes. To determine if alterations in serotonin levels could mimic changes in emotionality and social cohesiveness which follow lesions in the forebrain septum, normal rats were injected with p-CPA, methysergide, or control solutions. Although p-CPA, which depletes serotonin, induced the behavioral changes reported after lesions in the septum, blockage of serotonin receptors with methysergide did not. The results suggest that the effects of p-CPA on social behavior may not be due to changes in serotonin systems alone, but may result from the less dramatic depletions of norepinephrine produced by p-CPA, or a more complex relationship produced by p-CPA. A more complex relationship between serotonin, norepinephrine and other neurotransmitters is suggested. 12 references. (Author abstract modified)

001465 Danguir, Jaber; Nicolaidis, Stylianos; Perino-Martel, Marie-Christine. Laboratoire de Neurobiologie des Régulations, Collège de France, 75231 Paris Cedex 05, France **Effects of lithium chloride on sleep patterns in the rat.** Pharmacology Biochemistry and Behavior. 5(5):547-550, 1976.

The effects of lithium chloride on sleep patterns in the rat were investigated via continuous EEG recordings performed after saline injections (control days) and after lithium chloride treatments. Low toxic doses of lithium produced an initial period of general distress and sleep inhibition lasting 2 hr to 3 hr after administration. After high toxic doses, the effect persisted up to 10 hr. Once this state was overcome, lithium appeared to potentiate total sleep time and paradoxical sleep (PS). The potentiation of PS appears to occur as blood levels of lithium reach those used in human therapeutics. 11 references. (Author abstract modified)

001466 Danneskiold-Samsøe, P.; Pedersen, V. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ørttilavej 7-9, DK-2500 Copenhagen-Valby, Denmark **Inhibition of conditional avoidance response by neuroleptics upon repeated administration.** *Psychopharmacology* (Berlin). 51(1):9-14, 1976.

The development of tolerance to neuroleptic induced inhibition of avoidance behavior was studied in rats. Rats were pretreated for approximately 2 weeks with chlorprothixene, flupenthixol, fluphenazine, haloperidol, or piflutixol. Three days after withdrawal, single doses of chlorprothixene and flupenthixol caused a slightly but significantly weaker inhibition of avoidance performance and a shortened duration of effect in pretreated animals. Six days after withdrawal of piflutixol, the duration of effect of a single dose was significantly shortened. No homologous tolerance was demonstrated in fluphenazine pretreated rats. Cross tolerance was found after haloperidol pretreatment when the rats were tested with fluphenazine 6 days after withdrawal. Homologous piflutixol tolerance was demonstrated 4 weeks after withdrawal. Possible causes of the tolerance are discussed. 15 references. (Author abstract modified)

001467 Dantzer, R. I.N.R.A., Station de Pharmacologie-Toxicologie, 180 Chemin de Tournefeuille, F-31300 Toulouse, France. **Effect of diazepam on performance of pigs in a progressive ratio schedule.** *Physiology & Behavior*. 17(1):161-163, 1976.

The effect of diazepam on food motivation was studied in pigs using a progressive ratio schedule for food reinforcement. The number of responses in the final completed ratio, defined as the breaking point (Hodos, 1961) was used as a sensitive measure of food motivation. Diazepam increased the breaking point. The effect of diazepam was more important than that produced by changes in food motivation. 8 references. (Author abstract modified)

001468 Dawes, P.; Redfern, P. H. School of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, England **Changes in the conditioned avoidance behaviour of rats following the administration of drugs to the amygdala.** *Journal of Pharmacy and Pharmacology* (London). 28(Supplement):36P, 1976.

Research on the hypothesis that facilitation of conditioned avoidance with drugs such as amphetamine is specifically the result of an action on dopaminergic mechanisms is presented. Cannulae were stereotactically implanted in the central amygdaloid nucleus of male Sprague-Dawley rats. Drugs were injected 35 min before each training session. The training sessions consisted of 10 trials of a 5 sec sound followed immediately by a 5 sec, 70 volt shock applied to the cage floor, and training was done on 5 consecutive days. Drugs which mimicked or potentiated dopaminergic activity, i.e. the lower doses of amphetamine, apomorphine, and the dopamine uptake blocker benzotropine, all increased the mean occurrence of conditioned avoidances, while higher doses reduced condi-

tioned avoidances. The results suggest involvement of both dopamine and norepinephrine in the processes underlying avoidance behavior. 1 reference.

001469 Delbarre, B.; Schmitt, H.; Senon, Danielle. Département de Pharmacologie, Faculté de Médecine Broussais, 15, rue de l'Ecole de Médecine, F-75270 Paris Cedex 6, France **Effects of activation of H1- and H2-receptors on central cardiovascular structures in cats and on behaviour in chickens.** *British Journal of Pharmacology* (London). 58(3):443P-444P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of drug activation of H1-receptors and H2-receptors on central cardiovascular structures in cats and on behavior in newborn chickens. Histamine, pyridine and betahistine injected into the lateral ventricle of a cat brain induced hypertension and tachycardia, suggesting involvement of H1-receptors. These effects were suppressed by intraventricular administration of mepyramine but not metiamide. 4-Methylhistamine administered intraventricularly induced brief hypertension at low doses and hypotension at higher doses. These effects were abolished by metiamide and mepyramine. Histamine in newborn chicks induced sleep with loss of righting reflex. 4-Methylhistamine induced sleep for a shorter duration, and pyridine and betahistine failed to abolish the righting reflex. The results indicate a predominant role for H1-receptors for the stimulation of central cardiovascular structures but H2-receptors playing the primary role in inducing sleep in chickens. 2 references.

001470 Dews, P. B. Laboratory of Psychobiology, Harvard Medical School, Boston, MA **Effects of drugs on suppressed responding.** *British Journal of Pharmacology* (London). 58(3):451P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of drugs on suppressed responding in monkeys to assess the validity of using noxious punishment in experiments designed to test drug induced behavior. A nonnoxious stimulus, a white light, was used to suppress responding. Responding in the presence of the white light was increased by chlordiazepoxide and pentobarbital but not by chlorpromazine or methamphetamine, thus being affected by drugs similar to responding suppressed by electric shock. It appears that the selectivity of the drugs depends on the characteristics of the controls of the responding and not on the fear and anxiety engendered by electric shocks. It is suggested that the interpretation of conflict and punishment situations may be misleading. 3 references.

001471 Dobrzanski, S.; Doggett, N. S. Department of Applied Pharmacology, Welsh School of Pharmacy, UWIST, Cardiff, Wales **Studies in mice on the antagonism of dextroamphetamine anorexia by alpha-methyl-para-tyrosine methyl ester HCl.** *Neuropharmacology* (Oxford). 15(10):619-623, 1976.

The roles of dopamine (DA) and noradrenaline (NA) in the production of dextroamphetamine anorexia and in its antagonism by alpha-methyl-para-tyrosine methyl ester were investigated in mice. Anorexia resulting from dextroamphetamine pretreatment was potentiated by intracerebroventricular injection of DA and NA. Neither catecholamine produced any anorectic effects when given alone. The anorexia produced by dextroamphetamine was antagonized by alpha-methyl-para-tyrosine methyl ester. The submaximal antagonism produced by lower doses of the ester was

reversed by dihydroxyphenylalanine (DOPA) and by intracerebroventricular DA. NA failed to produce this reversal. It is suggested that, although both DA and NA may be involved in amphetamine induced anorexia and in its antagonism by alpha-methyl-para-tyrosine, the noradrenergic component is dependent upon a fully functional dopaminergic system. 27 references. (Author abstract modified)

001472 Dobrzanski, S.; Doggett, N. S. Department of Applied Pharmacology, Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cardiff, Wales **On the relation between hypodipsia and anorexia induced by (+)-amphetamine in the mouse.** *Journal of Pharmacy and Pharmacology* (London). 28(12):922-924, 1976.

The acute effects of (+)-amphetamine on drinking were studied in male albino C57BL/6J strain 1 mice who were water deprived. The mice were deprived of water from 5 p.m. to 2 p.m. the following day, and the effect of drugs on the amount of water consumed between 2 and 3 p.m. was measured when the mice had free access to food and when food was removed during the drinking period. Amphetamine produced a dose dependent depression of water intake. The effect of amphetamine was reversed by alpha-methyl-p-tyrosine. The mice who were deprived of food when allowed free access to water had a smaller water intake than the mice who had food available. Amphetamine reduced food intake and alpha-methyl-p-tyrosine reversed the anorectic effect of amphetamine. Low doses of amphetamine, which significantly depressed water intake of the mice when food was available, failed to do so in its absence. It is suggested that only at high doses that amphetamine induces hypodipsia independently of anorexia. 13 references.

001473 Douglas, Robert J.; Truncer, Philip C. Psychology Department, University of Washington, Seattle, WA 98105 **Parallel but independent effects of pentobarbital and scopolamine on hippocampus-related behavior.** *Behavioral Biology*. 18(3):359-367, 1976.

The effects of pentobarbital and scopolamine on hippocampus related behavior were investigated in rats to test the hypothesis that the barbiturates affect hippocampal circuits associated with entorhinal dentate gyrus input to this structure. In Wistar derived rats subanesthetic doses of pentobarbital were found to abolish spontaneous alternation, a form of exploratory behavior selectively sensitive to hippocampal damage and (until now) anticholinergic drugs. Pentobarbital completely abolished the behavior, as did scopolamine. Dose response curves for the two drugs could be closely superimposed on the assumption that the potency ratio was about 45:1. Combined injections of the two drugs, with each employed at barely subthreshold dosage, did not reliably reduce the alternation rate, although a superthreshold combination of the two drugs did completely abolish alternation. All effects were predicted on the basis of electrophysiological/pharmacological studies showing each drug to affect hippocampal electrical activity in a different way. Pentobarbital, scopolamine, and massive hippocampal lesions have now been found to have the same behavioral effects on at least five different and highly diagnostic responses. 13 references. (Author abstract)

001474 Dumeur, G.; Hue, Bernadette; Lwoff, J. M.; Mouriès, M. A.; Tremblay, D. Research Department, UPSA Laboratories, 128, rue Danton, F-92504 Rueil Malmaison, France **Activity of anorectic drugs (amphetamine), amfepramone and UP 507-04) on two models of obesity in animals.** *British Journal of Pharmacology* (London). 58(3):437P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the anorectic activity of amphetamine, amfepramone, and UP-507-04 on gold thioglucose treated mice and rats with bilateral electrolytic lesions of hypothalamic ventromedian nucleus. Amphetamine and UP-507-04 decreased food intake and bodyweight in both rats and mice while total lipids, triglycerides, and cholesterol levels did not change significantly. Amfepramone in mice had no activity on food intake and bodyweight.

001475 Eliasson, Mona; Meyerson, Bengt J. Dept. of Medical Pharmacology, University of Uppsala, Box 573, S-75123 Uppsala, Sweden **Comparison of the action of lysergic acid diethylamide and apomorphine on the copulatory response in the female rat.** *Psychopharmacology* (Berlin). 49(3):301-306, 1976.

The effects of lysergic acid diethylamide (LSD) and apomorphine were compared using female copulatory behavior (lordosis response), in ovariectomized estrogen plus progesterone treated rats. Both serotonin and dopamine are implicated in the inhibition of this behavior. Each compound inhibited lordosis behavior dose dependently and with a similar time course. Pimozide blocked the apomorphine induced decrease of lordosis response, while only a certain abbreviation of the LSD inhibition was achieved by pimozide. Chlorpromazine in a dose without effects on lordosis of its own had an action similar to pimozide on the LSD effect. It is concluded that the predominant action of LSD on the female copulatory response is not mediated by increased dopamine receptor activity but that the LSD effect might be modulated by decreased dopaminergic activity. 29 references. (Author abstract modified)

001476 Elmsore, Timothy F. Walter Reed Army Institute of Research, Washington, DC 20012 **The role of reinforcement loss in tolerance to chronic delta9-tetrahydrocannabinol effects on operant behavior of rhesus monkeys.** *Pharmacology Biochemistry and Behavior*. 5(2):123-128, 1976.

The reinforcement loss hypothesis of behavioral tolerance to the effects of delta9-tetrahydrocannabinol was investigated in rhesus monkeys. Two monkeys were trained on a multiple fixed-interval (FI), differential reinforcement of low rate (DRL) schedule of food reinforcement for lever pressing in which the two schedules, each correlated with a distinctive cue, alternated throughout an experimental session. Under chronic daily treatment with delta9-tetrahydrocannabinol, responding increased in both schedules. Performance on the DRL schedule was affected less dramatically than that on the FI schedule. Even though reinforcement frequency on the DRL schedule remained suppressed and FI reinforcement frequency was unaffected during chronic drug treatment, DRL performance showed greater tolerance than FI performance. Possible behavioral mechanisms which might account for these findings are discussed. 19 references. (Author abstract modified)

001477 Emery, Donna E.; Sachs, Benjamin D. Department of Psychology, University of Connecticut, Storrs, CT **Hormonal and monoaminergic influences on masculine copulatory behavior in the female rat.** *Hormones and Behavior*. 7(3):341-352, 1976.

Summaries of two experiments are presented. In the first, ovariectomized female rats receiving estradiol benzoate (EB), testosterone propionate, or no hormone treatment were administered parachlorophenylalanine (PCPA) alone or in combination with pargyline. Sixteen days of EB treatment resulted in hypertrophied pituitaries and concomitant pressure damage

to ventral portions of the brain. Irrespective of hormonal condition, females receiving PCPA treatment displayed more masculine copulatory behavior than females receiving PCPA plus pargyline or saline treatment. In the second study PCPA also potentiated masculine copulatory behavior in ovariectomized and adrenalectomized females receiving no hormone treatment. The ejaculatory pattern was observed in one of eight females receiving EB plus PCPA treatment and in two of seven ovariectomized and adrenalectomized females receiving PCPA treatment. The possible role of the hypothalamic pituitary-adrenal system in the expression of the ejaculatory pattern in male and female rats is discussed. 32 references. (Author abstract modified)

001478 Engel, Jorgen; Liljequist, Sture. Dept. of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg 33, Sweden The effect of long-term ethanol treatment on the sensitivity of the dopamine receptors in the nucleus accumbens. *Psychopharmacology* (Berlin). 49(3):253-257, 1976.

The effect of local application of dopamine into the nucleus accumbens on locomotor activity was studied in rats during and after withdrawal of long-term ethanol treatment. The bilateral application of dopamine into the nucleus accumbens of both the ethanol and withdrawal rats produced a pronounced increase in coordinated locomotor activity, which was 8 to 10 times higher than that of untreated water control rats. This effect of dopamine was antagonized by intraperitoneally administered haloperidol indicating a specific effect on dopamine receptors. It is concluded that prolonged ethanol administration may produce an increased sensitivity of the dopamine receptors in the nucleus accumbens and further support the contention that central catecholamine mechanisms are involved in the mediation of the withdrawal syndrome observed after long-term treatment with ethanol. 17 references. (Author abstract)

001479 Engelmann, Wolfgang; Bollig, I.; Hartmann, R. Institut für Biologie I, Universität Tübingen, Auf der Morgenstelle 1, D-7400 Tübingen, Germany /Effect of lithium ions on circadian rhythms./ Wirkung von Lithium-Ionen auf zirkadiane Rhythmen. *Arzneimittel-Forschung* (Aulendorf). 26(6):1085-1086, 1976.

The effect of lithium ion on the circadian rhythm in plants and animals is reviewed. It was found lithium ion lengthened the period during which the *Kalanchoe* plant blossom is open, and it also was found to lengthen the circadian rhythm period in the Meriones rat, and to alter the sleep/waking rhythm in canaries. 12 references.

001480 Evans, M. A.; Harbison, R. D.; Brown, D. J.; Forney, R. B. Department of Pharmacology, School of Medicine, Vanderbilt University, Nashville, TN 37232 Stimulant actions of delta9-tetrahydrocannabinol in mice. *Psychopharmacology* (Berlin). 50(3):245-250, 1976.

The stimulant actions of delta9-tetrahydrocannabinol (THC) on the behavior of mice were examined. THC augments the locomotor activity produced by methamphetamine in aggregated mice. THC induced augmentation was dose related and lasted for a 2 hour period. THC also increases locomotor activity among aggregated animals treated with saline. However, the increase was much less than the methamphetamine augmentation. In similar studies using isolated mice, THC produced only a dose related decrease in locomotor activity among both methamphetamine treated and saline treated animals. THC, 60mg/kg, had no effect on methamphetamine induced lethality in aggregated mice. However, at 15mg/kg,

THC significantly enhanced the lethality of methamphetamine. THC did not alter methamphetamine lethality in isolated mice. Distribution studies using ¹⁴C-methamphetamine indicated that neither THC nor isolation of animals affected tissue concentration or disappearance of ¹⁴C material. It is concluded that since THC at low doses can stimulate motor activity in saline treated animals, amphetamine may act only to amplify the behavioral activity produced by low doses of THC. 21 references. (Author abstract modified)

001481 Ezrin-Waters, C.; Muller, P.; Seeman, P. Department of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8 Catalepsy induced by morphine or haloperidol: effects of apomorphine and anticholinergic drugs. *Canadian Journal of Physiology and Pharmacology* (Ottawa). 54(4):516-519, 1976.

To investigate the extent of cholinergic involvement in opiate induced catalepsy, the effects of three anticholinergic drugs were studied on morphine induced catalepsy in rats. Haloperidol induced catalepsy was also examined. Maximum catalepsy in rats was obtained with 30mg/kg haloperidol. The anticholinergic drugs atropine, benztropine, and scopolamine were unable to antagonize morphine induced catalepsy, yet readily antagonized haloperidol induced catalepsy. Low doses of apomorphine, on the other hand, readily antagonized morphine catalepsy, but 13 fold higher doses of apomorphine were needed to block haloperidol induced catalepsy. The results are compatible with the idea that catalepsy can be mediated via the striatum or the amygdala; morphine dopamine antagonism may occur in the amygdala, whereas morphine dopamine holinergic interactions occur in the striatum. 27 references. (Author abstract)

001482 Fernandes, M.; Kluwe, S. Institut für Neuropsychopharmakologie, Freien Universität Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany /Relationship between physical dependence and tolerance of morphine in the rat./ Beziehungen zwischen physischer Abhängigkeit und Toleranz gegenüber Morphin bei der Ratte. *Arzneimittel-Forschung* (Aulendorf). 26(6):1100-1102, 1976.

Physical dependence and tolerance to morphine were studied in the rat, using the antagonist naloxone to quantify the amount of dependence. Tests used to measure morphine effect were catalepsy, the hotplate test, the acetic acid test, hyperthermia, inclined plane, lethality, emotional defecation, and time interaction. For the open-field test, parameters measured were number of crosses, amount of standing up, cleaning of paws, cleaning of mouth, resting, chewing, gnawing of paws, and licking of paws. Dose effect curves were plotted for the different morphine effects. Tolerance was dependent on dose and administration time, but this was not the case with dependence. Thus, in the rat, no correlation exists between tolerance and naloxone provoked withdrawal. 2 references.

001483 File, Sandra E. Pharmacology Department, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England A comparison of the effects of ethanol and chlordiazepoxide on exploration and on its habituation. *Physiological Psychology*. 4(4):529-532, 1976.

The effects of ethanol and chlordiazepoxide on exploration and habituation in rats placed in a four hole holeboard were studied. Low doses of ethanol (0.4g/kg) and chlordiazepoxide (5mg/kg) increased exploration by rats on trial 1 in a simple test situation, but the increase failed to reach significance when the situation was more complex. Ethanol (0.4g/kg) impaired response to a stimulus change since all groups except

this showed increased head dipping from trial 1 to trial 2 if objects were introduced on the second trial. Neither dose of ethanol impaired between trial habituation of exploration, but chlordiazepoxide (5mg/kg) retarded habituation, and chlordiazepoxide (7.5mg/kg) prevented it. While increased exploration might be ascribed to antianxiety actions of these drugs, impairments, specific to each drug, are also produced. 16 references. (Author abstract modified)

001484 File, Sandra E.; Hyde, J.; Pool, M. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Effects of ethanol and chlordiazepoxide on social interaction in rats.** *British Journal of Pharmacology* (London). 58(3):465p, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effects of ethanol and chlordiazepoxide on social interaction in rats. In low fear and high fear conditions ethanol did not significantly alter active social contact. However, in conditions of moderate fear, active contact increased. Chlordiazepoxide produced a dose related decrease in active social contact and an increase in passive contact. Both ethanol and chlordiazepoxide increased exploration, possibly due to anxiety reduction. 1 reference.

001485 Finch, A. A.; Reiter, L. W. U.S. Environmental Protection Agency, Health Effects Research Laboratory, Research Triangle Park, NC **Alterations in social behavior in the rat during chronic low-level exposure to lead and tritium.** *Toxicology and Applied Pharmacology*. 37(1):160, 1976.

The effects of chronic low level exposure to lead (Pb) and/or tritium (as tritiated water, HTO) on the social behavior of rats were investigated. Treated males were paired with weight matched controls and tested in a neutral observation chamber. Animals receiving high doses of HTO exhibited an increase in aggressive behavior; controls paired with this treatment group exhibited a corresponding increase in defensive behavior. Mutual social behavior was not altered in either group. Animals receiving high doses of Pb exhibited a decrease in aggressive behavior. Pb treatment produced no changes in pair interactions in either defensive behavior or mutual social behavior. Social behavior was not altered in animals receiving a combination of Pb and HTO. It is concluded that chronic low level exposure to either Pb or HTO produces changes in aggressive behavior in the rat. (Author abstract modified)

001486 Finney, Harry C.; Erpino, Michael J. Department of Biological Sciences, California State University, Chico, CA 95929 **Synergistic effect of estradiol benzoate and dihydrotestosterone on aggression in mice.** *Hormones and Behavior*. 7(4):391-400, 1976.

The effects of estradiol benzoate (EB), alone or in combination with dihydrotestosterone (DHT), on aggressive behavior in ovariectomized CD-1 male mice were investigated. EB in combination with DHT elicited aggression toward intact stimulus mice equivalent to that shown by intact (sham operated) animals and by testosterone treated animals. EB alone was less effective than EB with DHT. DHT alone elicited no more aggression than that observed in control animals. It is suggested that a synergism exists between EB and DHT in the central nervous system for the induction of aggressive behavior. 55 references. (Author abstract modified)

001487 Flexner, Josefa B.; Flexner, Louis B. Department of Anatomy, School of Medicine, University of Pennsylvania,

Philadelphia, PA 19174 **Effect of two inhibitors of dopamine beta-hydroxylase on maturation of memory in mice.** *Pharmacology Biochemistry and Behavior*. 5(2):117-121, 1976.

The possibility that the normal enlargement of the memory trace might be suppressed by creating an imbalance of neurotransmitters was investigated in mice. Bitemporal injections of puromycin that primarily affect the hippocampal/entorhinal cortical areas suppress memory of maze learning for 3 days after training. After 6 days, injections affecting widespread areas of the brain in addition to the hippocampal/entorhinal area are necessary for amnesia. It is suggested that the locus of the memory trace has enlarged at 6 days to include other parts of the CNS in addition to the hippocampal/entorhinal area. Mice treated for 7 days after training with inhibitors of dopamine-beta-hydroxylase, but not untreated controls, develop amnesia after bitemporal injections of puromycin. It is suggested that an imbalance of transmitters suppresses the normal enlargement of the locus of the memory trace. 20 references. (Author abstract modified)

001488 Fukuda, Sachio; Iwahara, Shinkuro. Department of Psychology, Tokyo University of Education, 3-29-1 Otsuka, Bunkyo-ku, 112 Tokyo, Japan **State-dependent learning produced by chlordiazepoxide and its transfer at different dose levels.** *Psychopharmacology* (Berlin). 48(2):193-198, 1976.

The contribution of chlordiazepoxide (CDP) as a stimulus in learning a shock motivated black/white discrimination task was investigated in rats. After a learning criterion was achieved in an animal with both drug administration and saline administration, the transfer gradient was tested with a single dose of CDP. Choice responses showed a bidirectional gradient around the training dose as in a stimulus generalization gradient. The transfer gradient was then tested with each animal receiving five different doses of CDP. The resulting transfer gradient was a single monotonic increasing function of dose levels. The discrepancy between the results obtained with one dose of drug and the results obtained with multiple drug doses is discussed. 10 references. (Author abstract modified)

001489 Gaddy, James R.; Neill, Darryl B. Department of Psychology, Emory University, Atlanta, GA 30322 **Enhancement of the locomotor response to d-amphetamine by olfactory bulb damage in rats.** *Pharmacology Biochemistry and Behavior*. 5(2):189-194, 1976.

The hypothesis that the olfactory bulbs may play an inhibitory role in some types of behavior was investigated in ovariectomized female rats. Bilateral removal of approximately 60% of the olfactory bulbs enhanced the locomotor response to d-amphetamine. The bulb damage did not reliably alter amphetamine induced stereotypy or anorexia. The results were interpreted as being consistent with the idea that the olfactory bulbs may exert an inhibitory influence over some aspects of behavior in rats. 37 references. (Author abstract modified)

001490 Gambill, John D.; Kornetsky, Conan. Department of Psychiatry, Boston University School of Medicine, 80 E. Concord Street, Boston, MA 02118 **Effects of chronic d-amphetamine on social behavior of the rat: implications for an animal model of paranoid schizophrenia.** *Psychopharmacology* (Berlin). 50(3):215-223, 1976.

In a study of the effects of chronic d-amphetamine on social behavior of the rat, hooded rats in a social colony were given increasing daily doses of d-amphetamine up to 8mg/kg. Timelapse cinematographically recorded behavior was analyzed for the following: grooming, feeding, sexual

behavior, sleeping, resting, stereotypy, agonistic behavior, suicidal activity, and the location and movement of each rat. Subordinate rats receiving d-amphetamine actively withdrew from social interactions by retreating to strategically defensible locations in the environment. They remained hypervigilant of other rats and overreacted to their approaches by either fleeing or by defensively rearing and boxing. On the other hand, when the dominant rat received the maximum dose, it seemed totally oblivious to the other rats. The responses to drug treatment in subordinate rats may provide a model for the social behavior of frightened paranoid schizophrenics. 16 references. (Author abstract)

001491 Gauron, Eugene F.; Rowley, Vinton N. no address
Use of a cross-over design in testing short-term methylphenidate effects on avoidance conditioning. *Psychological Reports*. 39(3, part2):1183-1187, 1976.

The use of a crossover design in testing short-term methylphenidate effects on avoidance conditioning was studied in 90 male and female rats. These were divided into 3 groups which received 4.5mg/kg, 13.5mg/kg, and an equal volume of distilled water respectively by injection for a total of 8 days. Following an initial avoidance conditioning period, one third of the animals remained on the training dosage while two thirds received the other two dosage combinations. Short-term administration of methylphenidate appeared to facilitate learning as measured by avoidance conditioning. No relationship was obtained between dosage level and response acquisition; however, a linear dose response relationship was obtained on activity level. The crossover design is seen as presenting advantages over other experimental designs in assessing a variety of possible drug effects. 7 references. (Author abstract modified)

001492 Gianutsos, Gerald; Hynes, Martin D.; Lal, Harbans. Department of Pharmacology, Michigan State University, E. Lansing, MI 48823 Enhancement of morphine-withdrawal and apomorphine-induced aggression by clonidine. *Psychopharmacology Communications*. 2(2):165-171, 1976.

The effects of clonidine, a proposed alpha-noradrenergic receptor stimulant, on aggression occurring during morphine withdrawal or following apomorphine administration were studied in rats. Clonidine intensifies the aggression induced by both conditions. The possibility of a noradrenergic/dopaminergic interaction in drug induced aggression is discussed. 14 references. (Author abstract modified)

001493 Gianutsos, Gerald; Lal, Harbans. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 Selective interaction of drugs with a discriminable stimulus associated with narcotic action. *Life Sciences*. 19(1):91-98, 1976.

A study was conducted to provide further evidence that the morphine discriminable cue is specific to narcotic drugs and that the stimuli are specifically prevented by narcotic antagonists. Rats were trained to bar press on either one of two levers depending on whether they received an injection of morphine or saline. The rats responded on the morphine correct lever when injected with another narcotic, fentanyl, but responded on the saline correct lever when injected with a narcotic antagonist or another CNS active, but nonnarcotic, drug, such as amphetamine or apomorphine. The narcotic antagonist naloxone prevented the occurrence of the narcotic discriminable stimulus, but the rats responded on the morphine correct lever when injected with morphine plus any of a number of potent CNS active, but nonnarcotic compounds. These results are discussed with reference to the specificity of

this procedure for detecting drugs with narcotic agonist or antagonist properties. 25 references. (Author abstract modified)

001494 Gilder, David A.; Fain, Wendy; Simpson, Lance L. Department of Pharmacology, College of Physicians and Surgeons, 630 West 168th St., New York, NY 10032 A comparison of the abilities of chlorpromazine and molindone to interact adversely with guanethidine. *Journal of Pharmacology and Experimental Therapeutics*. 198(2):255-263, 1976.

Chlorpromazine and molindone were tested for their abilities to impair conditioned avoidance behavior of rats. Chlorpromazine was effective within the dose range of 0.3 to 7.0mg/kg; molindone was effective with the range of 0.3 to 5.0mg/kg. Behaviorally relevant doses of chlorpromazine and molindone were then tested for their effects on blood pressure and on adrenergic mechanisms. When given intravenously to anesthetized, hypertensive animals, both drugs (1.0mg/kg) produced significant but transient vasodepression. When given intraperitoneally to anesthetized or to conscious hypertensive rats, the drugs did not produce significant effects on blood pressure. Both drugs (1.0mg/kg) blocked responses to an alpha agonist (methoxamine), but chlorpromazine was significantly more potent than molindone. In addition, chlorpromazine produced a dose-dependent (1.0-10.0mg/kg) inhibition of 3H-l-norepinephrine uptake into heart, but molindone at the same doses produced no inhibition of uptake. In related experiments, it was found that guanethidine (50 mg/kg) was an effective agent for lowering blood pressure of hypertensive rats. When chlorpromazine (3-10 mg/kg) was administered concomitantly with guanethidine, there was no loss of blood pressure control. It is concluded that molindone is an important drug, because it is an antipsychotic agent that does not interact adversely with guanethidine. 16 references. (Journal abstract)

001495 Goldberg, S. R.; Morse, W. H.; Goldberg, D. M. Harvard Medical School, New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772 Behavior maintained under a second-order schedule by intramuscular injection of morphine or cocaine in Rhesus monkeys. *Journal of Pharmacology and Experimental Therapeutics*. 199(1):278-286, 1976.

The effects of cocaine and morphine in maintaining behavior in three rhesus monkeys was studied independently of other behavioral effects. The experiments extend the range of conditions and parameters under which drug maintained behavior can be studied. Under the second order schedule of morphine injection, a low dose of nalorphine increased responding, while higher doses decreased responding. It is suggested that the factors responsible for the different situations should become clearer as nalorphine is studied under a wider variety of conditions. 34 references.

001496 Goldstein, Avram. Department of Pharmacology, Stanford University, Stanford, CA Opioid peptides (endorphins) in pituitary and brain. *Science*. 193(4258):1081-1086, 1976.

An overview of research on opioid peptides (endorphins) in the pituitary and brain and the implications of such research is presented. Summaries are given of studies on opiate receptors and their endogenous ligands, assay methods, and the characteristics of endorphins. The possible physiological role of endorphins is discussed in terms of the possibility that endorphin deficiency could play a role in narcotic addiction as well as in pain mechanisms and affective disorders. It is emphasized that research has great potential in these areas. 56 references. (Author abstract modified)

001497 Goldstein, Dora B.; Arnold, Virginia W. Department of Pharmacology, Stanford University School of Medicine, Stanford, CA **Drinking patterns as predictors of alcohol withdrawal reactions in DBA/2J mice.** *Journal of Pharmacology and Experimental Therapeutics.* 199(2):408-414, 1976.

The effects of alcohol intake upon withdrawal symptoms in mice was studied. DBA/2J mice fed a liquid diet in which ethanol supplied 33% of the calories showed increased severity of withdrawal reaction progressively with duration of alcohol administration as measured by scoring convulsions elicited by handling the mice after discontinuing the alcohol diet. Pretreatment of mice with alcohol in their drinking water slightly increased the subsequent intake of the liquid diet. Effective alcohol intake was defined as uninterrupted alcohol consumption above 10g/kg/day. Withdrawal scores correlated better with effective intake than with total intake under a variety of conditions. The results imply that brief interruptions in drinking may allow the accrued physical dependence to disappear. (Author abstract modified)

001498 Gordon, William C. S.U.N.Y., Binghamton, NY **Similarities between short-term and reactivated memories.** Final report, NIMH Grant MH-25760, 1976, 10 p.

The hypothesis that reactivated or retrieved information is reprocessed in the same manner as newly acquired information was tested in rats. Three series of experiments attempted to show that: 1) analeptic agents have the same effect on both types of information; 2) electroconvulsive shock and other disruptors such as "unexpected events" have the same effect on both types of information; and 3) both reactivated and newly acquired information interfere with retention of subsequently acquired information in the same manner. Rats were trained on a learning task, given some treatment intended to facilitate or interfere with retention of the task, and administered retention tests. Results of these procedures were then compared with those obtained when animals were trained, given a 1 to 3 day interval, given a reactivation or retrieval inducing treatment, and then administered a treatment thought to influence retention. Results indicate that: 1) support for the facilitative effects of analeptic agents on reactivated memory is not always apparent; 2) the use of electroshock disruption in the present context presents methodological difficulties; and 3) newly acquired and recently retrieved information both require similar active processing, and therefore are capable of interfering with the retention of new learning as long as this processing continues.

001499 Gray, Gary D.; Davis, Harry N.; Dewsbury, Donald A. Department of Physiology, Stanford University, Stanford, CA 94305 **Masculine sexual behavior in male and female rats following perinatal manipulation of androgen: effects of genital anesthetization and sexual experience.** *Hormones and Behavior.* 7(3):317-329, 1976.

A detailed behavioral analysis of the effects of androgen during perinatal development is presented. Twenty six androgenized female rats, 14 day 1 male castrates, 26 normal males, and 17 normal females were tested for mounting behavior as adults following administration of testosterone propionate (TP). Genital anesthetization was used to eliminate all intromission and ejaculation behavior. Results showed that sexually naive normal males and androgenized females mounted significantly more than day 1 male castrates, while day 1 male castrates mounted significantly more than normal females. Sexually experienced normal males and androgenized females displayed a significant facilitation of mounting behavior as compared to the sexually naive animals. Tests of

masculine copulatory behavior without genital anesthetization also were conducted with androgenized females and normal males, and the two groups were indistinguishable in all aspects of the complete masculine pattern. It is concluded that during perinatal development androgen may act directly on neural systems that will later regulate adult masculine sexual behavior. 40 references. (Author abstract modified)

001500 Green, R. A.; Barchas, J. D.; Elliott, G. R.; Carman, J. S.; Wyatt, R. J. William A. White Building, Room 536, Saint Elizabeths Hospital, IRP, NIMH, Washington, D.C. 20032 **The tryptolines: effect of intraventricular administration on spontaneous motor activity of rats.** *Pharmacology Biochemistry and Behavior.* 5(4):383-385, 1976.

The effects of intraventricularly administered tryptoline, 5-hydroxytryptoline and 5-methoxytryptoline on spontaneous motor activity were studied in rats and compared with the effects produced by the structurally similar compounds tryptamine, 5-hydroxytryptamine (serotonin, 5-HT) and 5-methoxytryptamine. Spontaneous motor activity decreased markedly after injections of the tryptolines as well as after injections of the tryptamines. Since both the tryptamines and the tryptolines have been shown to be inhibitors of 5-HT uptake, it is suggested that these compounds are acting indirectly through an effect on the serotonergic system. 16 references. (Author abstract modified)

001501 Green, R. A.; Gillin, J. C.; Wyatt, R. J. Laboratory of Clinical Psychopharmacology, National Institute of Mental Health, Saint Elizabeth's Hospital, Washington, DC 20032 **The inhibitory effect of intraventricular administration of serotonin on spontaneous motor activity of rats.** *Psychopharmacology (Berlin).* 51(1):81-84, 1976.

The effects of injection of serotonin (5-HT) into the lateral ventricle on spontaneous motor activity were studied in rats. During the first 15 min, the rats receiving 10 or 50 micrograms of 5-HT showed significant decrements in motor activity compared to saline controls. No activation was observed with either dose. After 20 min, no significant differences between treated rats and controls were found. It is concluded that a principal effect of increasing 5-HT concentration is to decrease activity. Possible mechanisms for this effect are discussed. 25 references. (Author abstract modified)

001502 Greindl, M. Gh.; Preat, S. UCB Pharmaceutical Division, Neuropharmacological Research, 68, Berkendael Street, B-1060, Brussels, Belgium **A new model of active avoidance conditioning adequate for pharmacological studies.** *Archives internationales de Pharmacodynamie et de Therapie (Ghent).* 223(1):168-170, 1976.

A model of rapid learning (active avoidance conditioning) using rats, which induces retention depending on the number of trials to which the animals are submitted, is described. For three trials (double stimulation) adequately spaced, the memory trace lasts for 48 hr., while six trials induce a trace for 10 days. One single application of double stimulation does not give any apparent retention in normal rats for 24 hr. This experimental fact was used to study and screen the activity of substances on the learning process. Animals treated with piracetam, pemoline, methamphetamine, strychnine, pyritinol, and meclofenoxate before this single trial, displayed evidence of retention 24 hr. later. Other substances with known clinical CNS activities (e.g., tranquilizers, analgesics, etc.) showed no positive effect on the memory trace. (Author abstract modified)

001503 Griffiths, Roland R.; Winger, Gail; Brady, Joseph V.; Snell, Jack D. Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Comparison of behavior maintained by infusions of eight phenylethylamines in baboons.** *Psychopharmacology (Berlin)*. 50(3):251-258, 1976.

In a comparison of behavior maintained by infusions of phenylethylamines in baboons, doses of eight phenylethylamines were substituted for cocaine on a drug maintained behavior baseline. Intravenous infusions of drug were contingent upon completion of 160 lever presses. Fenfluramine was the only drug that did not maintain self-infusion performance at any dose tested. d-Amphetamine was approximately 10 times more potent than phentermine, phenmetrazine or diethylpropion, and 20 to 30 times more potent than methylenedioxymphetamine (MDA), chlorphentermine or chlorphentermine, in maintaining self-infusion behavior. Some doses of d-amphetamine and phentermine produced a cyclic pattern of drug intake over days. Increasing self-infused doses of all drugs produced a substantial suppression of concurrent food maintained behavior. There was no clear relation between the potency of the phenylethylamines in maintaining self-infusion performance and the potency in suppressing food maintained behavior, which indicates that different mechanisms may underlie the two effects. Examination of chemical structures indicates that substitution on the phenyl ring may decrease the potency of phenylethylamines in maintaining self-infusion behavior.

001504 Gunne, Lars-M.; Barany, Sven. Psychiatric Research Center, S-750 17 Uppsala, Sweden **Haloperidol-induced tardive dyskinesia in monkeys.** *Psychopharmacology (Berlin)*. 50(3):237-240, 1976.

Behavioral disturbances in three chronically haloperidol treated monkeys were examined. In three cebus monkeys the chronic daily administration of haloperidol created sedation and parkinsonism during the first 5 to 7 weeks. Later the animals developed signs reminiscent of acute dystonia, as seen in the clinic during treatment with neuroleptics. These signs were dose dependent and in extreme cases included widespread tonic and clonic seizures. After 3 and 12 months, respectively, two of the cebus monkeys developed buccolingual signs (grimacing and tongue protrusion), similar to tardive dyskinesia in the clinic. The tardive dyskinesia symptoms were reduced in a dose dependent manner after each haloperidol administration, being most pronounced in the morning before haloperidol was given. Biperiden reduced acute dystonia but reinstated signs of tardive dyskinesia, which had been abolished by haloperidol. It is suggested that cebus monkeys may provide a useful animal model for the study of neurologic long-term complications from neuroleptic drugs. 11 references. (Author abstract)

001505 Hadorn, David; Mandell, Arnold J.; Segal, David S. University of California, San Diego, La Jolla, CA 92037 **The effects of chronic mescaline administration on operant behavior in the pigeon.** *Behavioral Biology*. 17(3):403-409, 1976.

In order to determine the effects of chronic mescaline administration on fixed ratio appetitive responding, a dose of 6.5mg/kg was administered to 14 pigeons. The results indicate that this dose, which acutely abolishes fixed ratio appetitive responding in pigeons becomes progressively less disruptive with repeated administration. When responding reaches about 60% of baseline (in about three weeks) no further tolerance occurs. A dose of 3.5mg/kg mescaline acutely lowers responding to about 60% of baseline and repeated administration of

this dose continues to produce approximately the same response deficit. Discontinuation of both doses results in an immediate return to baseline levels of responding. Two possible mechanisms underlying this two stage action of mescaline seen in this and other studies are discussed. The endogenous hallucinogen hypothesis of schizophrenia is considered in light of the existence of tolerance resistant hallucinogenic drug effects. 20 references. (Author abstract modified)

001506 Harston, Craig T.; Sibley, David H.; Gallup, Gordon G., Jr.; Wallnau, Larry B. Tulane University, New Orleans, LA 70118 **Effects of intraventricular injections of imipramine and 5-hydroxytryptamine on tonic immobility in chickens.** *Bulletin of the Psychonomic Society*. 8(5):403-405, 1976.

Two experiments were designed to clarify the effect of centrally administered serotonin and to resolve paradoxical results of imipramine by investigating the effects of these compounds on tonic immobility in chickens following intraventricular administration. While previous work has shown that peripherally administered serotonin and imipramine attenuate tonic immobility in chickens, in the present study with 28 chickens, intraventricular application of these compounds served to prolong the reaction. Data are discussed in terms of the possibility of an inverse relationship between raphe electrical activity and the duration of tonic immobility in chickens. 19 references. (Author abstract modified)

001507 Harting, J.; McMillan, D. E. Medical Research Division, E. Merck, Darmstadt, Germany, P. O. Box 4119, 61 Darmstadt, Germany **Effects of pentobarbital and d-amphetamine on the repeated acquisition of response sequences by pigeons.** *Psychopharmacology (Berlin)*. 49(3):245-248, 1976.

The effects of d-amphetamine and pentobarbital on the acquisition of position sequences under chained and tandem schedules with reset contingencies were studied, and these drug effects were compared with those obtained under similar schedules without reset contingencies (nonreset). Pigeons were trained to acquire a new four response sequence in each session by pecking three keys in a predetermined order. The key color varied for each step under the chained schedule, but there was only one key color under the tandem schedule. Under the reset contingency, incorrect responses produced a reset of the four response sequence to its beginning and a short timeout. In the nonreset contingency, only the timeout was produced by incorrect responses. Under both contingencies of both schedules, low doses of pentobarbital increased the response rate and the total number of errors, although the rate increases usually occurred at lower doses than did the increases in errors. A dose of 17.5mg/kg pentobarbital eliminated almost all responding. Injection of low doses of d-amphetamine decreased the total number of errors under both contingencies of both the chained and the tandem schedules. Higher doses of d-amphetamine sometimes increased the total number of errors and decreased the response rate. 7 references. (Author abstract modified)

001508 Heninger, George R.; Sheard, Michael H. Connecticut Mental Health Center, New Haven, CT 06519 **Lithium effects on the somatosensory cortical evoked response in the rat and cat.** *Life Sciences*. 19(1):19-27, 1976.

A study was carried out to determine whether the increase in amplitude of the early positive cortical evoked potential to somatosensory stimuli which occurs in humans receiving lithium chloride treatment also occurs in the rat and/or the cat. Cortical evoked potentials to peripheral somatosensory stimulation were obtained in rats and cats with implanted epidural

electrodes. In rats, increasing doses of oral lithium chloride produced no reliable change in the early positive evoked response amplitude. In cats, an increased amplitude of the early positive negative cortical potential was observed in every instance, and the serum lithium levels were within the range used clinically in humans. The increased cortical evoked response amplitude in cats did not directly correlate with serum lithium levels but was delayed 1 to 5 days after serum lithium levels reached their peak. The findings in cats are similar to the human studies. The negative results observed in rats may reflect important species differences regarding lithium. 21 references. (Author abstract modified)

001509 Herman, Z. S.; Drybanski, A.; Trzeciak, H. I. Dept. of Pharmacology, Biological Physiological Inst., Silesian School of Medicine, PL-41-808, Zabrze, Poland **Increased aggression in rats after withdrawal of long term used oxazepam.** *Experientia* (Basel). 32(10):1305-1306, 1976.

In light of conflicting data on the antiaggression activity of oxazepam, the effects of long-term use and subsequent withdrawal of this drug on aggression in rats were investigated. Male Wistar rats were treated for a year with 5mg/kg i.p. oxazepam daily except Sundays. Control rats received sodium chloride injections. Aggressive behavior was induced by applying footshocks to the rats, and test sessions consisted of 50 shocks. Results indicate that oxazepam had no effect on shock induced aggression from 2 to 24 hours after treatment. Withdrawal of the drug for 48 hours or more increased aggression. It is concluded that long-term administration of oxazepam can cause dependency in rats, although it is noted that the effect of the drug on aggression can vary with the experimental model of aggression used.

001510 Herndon, James G., Jr. Yerkes Regional Primate Research Center, Emory University, Atlanta, GA 30322 **Effects of midbrain lesions on female sexual behavior in the rat.** *Physiology & Behavior*. 17(1):143-148, 1976.

The effects on female sexual behavior of selective depletion of the monamine content in the forebrain induced by lesions of the appropriate pathways in the midbrain were studied in the rat. Severe deficits in receptivity were produced by lesions aimed at the dorsal norepinephrine (NE) pathway and the ventral NE pathway (DV) (DV lesions) and by lesions intended to destroy mesolimbic (A-10) dopamine (DA), producing cells. Significant but less profound impairments were seen following lesions aimed at the serotonin (5-hydroxytryptamine, 5-HT) producing raphe nucleus or the nigrostriatal DA cells. Systemically administered dextroamphetamine increased receptivity in severely impaired A-10 animals and DV animals. It is proposed that the observed deficits may result from damage to midbrain structures involved in the sensory/motor mediation or hormonal mediation of the lordosis reflex, or from disruption of a neurochemical system involved in control of lordosis. 22 references. (Author abstract modified)

001511 Hicks, Lou E. Department of Psychology, University of New Orleans-Lakefront, New Orleans, LA 70122 **Effects of anticholinergics on the habituation of tonic immobility in chickens.** *Behavioral Biology*. 18(2):199-109, 1976.

To test expectations derived from Carlton's general theory of cholinergic action which states that anticholinergics in general antagonize habituation, two experiments were conducted. Experiment 1 determined the effect of 12.2 or 24.5mg/kg of atropine, 0.5 or 0.9mg/kg of scopolamine, or saline, on the duration of the tonic immobility (TI) response in White Leghorn chickens. Scopolamine injections markedly

reduced TI duration, while atropine had no effect, suggesting that different anticholinergics may have differential effects on fear potentiated responses. Experiment 2 investigated the effects of scopolamine (0.5mg/kg), methylscopolamine (0.5mg/kg), or saline injections on the habituation of susceptibility to TI. There were indications that scopolamine served to facilitate, not antagonize, the habituation of this response. 33 references. (Author abstract)

001512 Hiley, C. R. Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool L69 3BX, England **Ontogenesis of muscarinic receptor sites in rat brain.** *British Journal of Pharmacology* (London). 58(3):427P-428P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the ontogenesis of muscarinic receptor sites in the rat brain. Cholinergic neurotransmission in the central nervous system does not appear to be fully functional until the second week of life. Rats do not respond to injections of scopolamine with locomotor activity changes until after the 15th day of life, and the synergistic effect of scopolamine on amphetamine induced gnawing in 30-day-old rats could not be seen in 10-day-old rats. Homogenates of cerebral cortex and caudate nucleus incubated with tritiated atropine and treated with propylbenzylcholine gave results indicating that the lack of response to scopolamine in young rats is probably not a consequence of the absence of the muscarinic cholinergic receptor although it is possible that the receptor is not functionally connected to processes responsible for changes mediated by cholinergic agents. 3 references.

001513 Hill, Shirley Y.; Powell, Barbara J. Department of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63110 **Acquired preference for morphine but not d-amphetamine as a result of saccharine adulteration.** *Psychopharmacology* (Berlin). 50(3):309-312, 1976.

The consumption of morphine sulfate and d-amphetamine was studied in two groups of rats. In a choice situation, preference for both drugs remained low after 46 days of drinking. In two additional groups morphine and d-amphetamine solutions were prepared with 1% saccharine. Morphine drinking was significantly increased by saccharine adulteration, whereas drinking of amphetamine solutions decreased. Addition of saccharine to morphine solutions increased drinking in more than a simple additive way. Saccharine facilitates the acquisition of drug directed behavior. The slope of the acquisition trails for the morphine saccharine group was significantly different from horizontal (0 slope) and significantly different from the slope found for the morphine without saccharine group. 13 references. (Author abstract)

001514 Hole, Kjell; Fuxe, Kjell; Jonsson, Gosta. Institute of Physiology, University of Bergen, Norway **Behavioral effects of 5,7-dihydroxytryptamine lesions of ascending 5-hydroxytryptamine pathways.** *Brain Research* (Amsterdam). 107(2):385-399, 1976.

Some behavioral effects of 5,7-dihydroxytryptamine (5,7-DHT) lesions of the medial 5-hydroxytryptamine (5-HT) bundle and/or the lateral 5-HT bundle in the mesencephalon were studied in rats. Lesions of both bundles increased 5-HT fluorescence in these bundles and reduced the in vitro uptake of radiolabeled 5-HT in the hypothalamus in the cortex cerebri. Selective lesioning of the medial 5-HT bundle reduced 5-HT uptake both in hypothalamus and in cortex cerebri, while

selective lesioning of the lateral 5-HT bundle significantly reduced 5HT uptake only in the cortex. Locomotor activity in an open field was significantly reduced by lesions in both bundles. 5-Hydroxytryptophan and a peripheral decarboxylase inhibitor postoperatively induced a pronounced behavioral 5-HT syndrome in rats with lesions of both bundles. Pain sensitivity, morphine analgesia and acquisition of a one way avoidance response were unchanged, and apomorphine induced locomotor activity and stereotyped behavior were unaffected. It is concluded that the medial 5-HTC bundle innervates both the hypothalamus and the cortex cerebri and the lateral 5-HT bundle innervates mainly the cortex. 54 references. (Author abstract modified)

001515 Hughes, R. N.; Greig, Andrea M. Department of Psychology, University of Canterbury, Christchurch, New Zealand **Effects of caffeine, methamphetamine and methylphenidate on reactions to novelty and activity in rats.** *Neuropharmacology* (Oxford). 15(11):673-676, 1976.

Observations were made of the effects of three doses of caffeine, methamphetamine, and methylphenidate on ambulation, rearing, and novelty preferences in hooded rats. All three drugs produced inverted U-shaped dose response curves for ambulation and U-shaped curves for novelty preference. Whereas both methamphetamine and methylphenidate increased rearing, this response was totally unaffected by caffeine. The results are discussed in terms of the classification of central behavioral effects of the drugs and their modification of motor activity and exploratory behavior. 28 references. (Author abstract)

001516 Hughes, R. N.; Trowland, R. Department of Psychology, University of Canterbury, Christchurch 1, New Zealand **Physostigmine effects on activity and reactions to novelty.** *Life Sciences* (Oxford). 19(6):793-796, 1976.

Effects of doses of physostigmine on reactions to novelty, rearing, and ambulation in rats were observed in an exploration box which allowed free choice of novel and familiar halves. All responses tended towards decreases with higher doses, but whereas this trend was significant for rearing and ambulation, it was only suggestive for reactions to novelty. The results were discussed in the light of views on cholinergically controlled habituation processes. It is concluded that in the present experimental setting, the effects of neither scopolamine nor physostigmine support cholinergic involvement in responsiveness to novel stimuli. Findings described further question the validity of single process interpretations of behavioral effects of cholinergically active drugs. 18 references. (Author abstract modified)

001517 Jacobs, Barry L.; Trulson, Michael E. Department of Psychology, Princeton University, Princeton, NJ 08540 **An animal behavior model for studying the actions of LSD and related hallucinogens.** *Science*. 194(4266):741-743, 1976.

An animal based model for studying the behavioral effects of hallucinogens, based on the observed behavior of cats after injection of d-lysergic acid diethylamide (LSD), is proposed. Two of the observed behaviors, limb flick and abortive grooming, have a very low frequency of occurrence in normal cats, but often dominate the behavior of LSD treated cats. The frequency of these behaviors is related to LSD dosage. The behavioral changes are long lasting following a single injection of LSD, and exhibit tolerance following the repeated administration. They are not elicited by a variety of control drugs, but are elicited by other indole nucleus hallucinogens. Because the behavioral effects are specific, reliable, easy to score, and

quantifiable, they represent an animal model that can be used in studies of the effects of LSD and related hallucinogens. 13 references. (Author abstract modified)

001518 Jarbe, T. U. C.; Johansson, J. O.; Henriksson, B. G. Department of Psychology, University of Uppsala, Box 227, S-75104 Uppsala, Sweden **Characteristics of tetrahydrocannabinol (THC)-produced discrimination in rats.** *Psychopharmacology* (Berlin). 48(2):181-187, 1976.

The effects of several doses of tetrahydrocannabinol (THC) on the amount of training required to establish drug discrimination response in a T-maze were studied in rats. Pentobarbital induced discrimination was investigated for comparison purposes. The effects of pretreatment with alpha-methyl-p-tyrosine (AMPT) and p-chlorophenyl-alanine (PCPA) on THC induced discrimination were also studied. Animals required to differentiate high doses of THC from no drug acquired the T-maze task faster than animals trained with lower doses of THC. It is suggested that delta8-THC is less effective than delta9-THC in producing state dependency. Hashish smoke can maintain drug responding among THC trained rats. A lowering of brain catecholamine levels and/or serotonin levels induced by AMPT and PCPA did not reduce delta9-THC discrimination. 54 references. (Author abstract modified)

001519 Jenner, P. G.; Pycock, C. J. University Department of Neurology, King's College Hospital Medical School, Denmark Hill, London SE5 8AF, England **Interaction of clonidine with dopamine-dependent behaviours in rodents.** *British Journal of Pharmacology* (London). 58(3):469P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effect of clonidine on dopamine dependent behaviors in rodents. Clonidine potentiated circling behavior induced by both apomorphine and amphetamine in mice with unilateral destruction of the nigrostriatal dopaminergic pathway. It also enhanced apomorphine induced reversal of reserpine akinesia in mice, and potentiated apomorphine induced hyperactivity in rats. Clonidine was without effect on apomorphine induced stereotypy in rats. The results suggest that clonidine significantly modifies all dopamine dependent behaviors having a motor component such as circling behavior and locomotor activity, but apparently fails to influence stereotypy or to directly affect striatal dopaminergic mechanisms, and thus does not influence all forms of dopamine mediated behavior. 2 references.

001520 Johnson, F. N. Dept. of Psychology, University of Lancaster, Lancaster LA1 4YF, England **Lithium effects on vertical activity in rats: a reply to D. F. Smith.** *Experientia* (Basel). 32(10):1350-1351, 1976.

The Johnson hypothesis that the effects of lithium on vertical rearing behavior in rats are mediated by environmental factors is defended. It is contended that in the Johnson studies lithium did not produce tissue damage which was observed in Smith's (1976) study, and that discrepancies in results may be partially explained by the different strains of animals used. The necessity of measuring varying dose levels of lithium is emphasized, and the benefits of several analytic methods are briefly outlined. It is contended and concluded that the behavioral effects of lithium are, in fact, influenced by environmental factors and that this would have been evidenced in Smith's studies had they been conducted properly. 12 references.

001521 Jones, Byron C.; Consroe, Paul F.; Laird, Hugh E., II. Department of Pharmacology and Toxicology, College of Pharmacy, University of Arizona, Tucson, AZ 85721 **The interaction of delta9-tetrahydrocannabinol with cholinomimetic drugs in an agonist-antagonist paradigm.** *European Journal of Pharmacology* (Amsterdam). 38(2):253-259, 1976.

The interactions between delta9-tetrahydrocannabinol (delta9-THC) and physostigmine, arecoline and nicotine were examined in rabbits. The cholinomimetics effectively reversed the cortical EEG alterations and hippocampal EEG alterations induced by delta9-THC. Arecoline and physostigmine temporarily reversed the behavioral effects and sedative effects of delta9-THC, whereas nicotine produced behavioral collapse preceded by behavioral disturbance. 14 references. (Author abstract modified)

001522 Kafi, Sarah; Gaillard, Jean-Michel. Clinique Psychiatrique de l'Université de Genève, Bel-Air, CH-1225, Chêne-Bourg, Switzerland **Brain dopamine receptors and sleep in the rat: effects of stimulation and blockade.** *European Journal of Pharmacology* (Amsterdam). 38(2):357-364, 1976.

The influence on sleep of pharmacological substances acting on dopamine (DA) metabolism or DA receptor activity was studied in rats. Apomorphine, a stimulator of brain DA receptors, caused a reduction in total sleep and intermediate sleep and a delayed appearance of paradoxical sleep. Lower doses of apomorphine produced a small and not significant trend toward an increase of paradoxical sleep. Spiroperidol, a specific blocker of DA receptors, produced a dose dependent increase of total sleep and a decrease of paradoxical sleep. Chlorpromazine produced a clear enhancement of paradoxical sleep. It is suggested that an activation of DA systems in the brain is partly involved not only in behavioral activation, but also in cortical activation of waking and paradoxical sleep. The effect of chlorpromazine on paradoxical sleep cannot be attributed to the antidopaminergic properties of the drug. 30 references. (Author abstract modified)

001523 Kameyama, Tsutomu; Shigehisa, Tsuyoshi; Nabeshima, Toshitaka. Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Effects of imipramine on auditory sensitivity in the rat in relation to initial sensitivity.** *Psychopharmacology* (Berlin). 48(2):199-204, 1976.

The effects of imipramine on auditory sensitivity in the rat were studied in order to investigate the hypotheses that the observed differences in the effects of imipramine in animals and in humans are related to: 1) dosage and temporal parameters; 2) initial level of activity or type of subject; and 3) stimulus receptivity. It was found that: 1) imipramine increases absolute auditory sensitivity in the rat whose initial sensitivity is relatively low, and decreases auditory sensitivity in the rat whose initial sensitivity is initially relatively high; 2) the lower the initial auditory sensitivity, the greater the increase in sensitivity after imipramine; and 3) the effects of imipramine on auditory sensitivity, both inhibitory and facilitory, vary with the dosage and with time after administration. 35 references.

001524 Karpov, V. N. Chitinskogo meditsinskogo instituta, Chita, USSR **/Chlorpromazine and haloperidol action on caudate inhibition of conditioned reflex avoidance reaction in cats./** *Vliyanie aminazina i galoperidola na kaudatnoye tormozheniye uslovnoreflektornoy reyaktsii izbeganiya u koshek. Farmakologiya i Toksikologiya* (Moskva). 2:141-144, 1976.

The effect of neuroleptics on avoidance behavior during low frequency electrical stimulation of the caudate nucleus was studied in experiments with 7 adult cats. Chlorpromazine and haloperidol disordered the behavior of the animals and intensified the inhibitory function of the caudate nucleus. Chlorpromazine proved to be a more active substance. The results obtained may be attributed to disruption of the central dopamine and noradrenergic transmission. 7 references. (Author abstract modified)

001525 Katz, R. J.; Thomas, E. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Effects of para-chlorophenylalanine upon brain stimulated affective attack in the cat.** *Pharmacology Biochemistry and Behavior*. 5(4):391-394, 1976.

The effects of parachlorophenylalanine (PCPA) on affective attack behavior elicited by electrical stimulation of the ventromedial hypothalamic nucleus were studied in the cat. Potentiation of affective attack patterns was observed for a number of the components of attack behavior (approach, use of forepaws, and biting), and a criteria was established for scaling each category. PCPA produced potentiation in measures of attack, with three of five measures reaching statistical significance. It is suggested that there may be serotonergic involvement in the inhibitory control of several aspects of affective attack. 28 references. (Author abstract modified)

001526 Kelly, Peter H.; Iversen, Susan D. Department of Experimental Psychology, Downing Street, Cambridge, England **Selective 6OHDA-induced destruction of mesolimbic dopamine neurons: abolition of psychostimulant-induced locomotor activity in rats.** *European Journal of Pharmacology* (Amsterdam). 40(1):45-56, 1976.

The abolition of psychostimulant induced locomotor activity in rats following selective destruction of mesolimbic dopamine neurons by 6-hydroxydopamine (6OHDA) was studied. 6OHDA was injected into the nucleus accumbens septi in rats pretreated with pargyline and desipramine preventing the destruction of the noradrenergic innervation of the forebrain without affecting the destruction of dopamine containing neurons. Locomotor activity stimulation produced by amphetamine and cocaine was inhibited by this destruction while locomotor stimulation produced by apomorphine was enhanced. This may indicate supersensitivity of the denervated dopamine receptors. The data seem to support the view that psychostimulant induced locomotor activity stimulation in rats results from effects on mesolimbic dopamine neurons. In addition, protection of noradrenergic neurons by desipramine from the toxic effects of 6OHDA suggests that 6OHDA destroys catecholamine neurons mainly by an uptake dependent specific mechanism. 29 references. (Author abstract modified)

001527 Kelsey, John E. Department of Psychology, Indiana University, Bloomington, IN 47401 **Behavioral effects of intraseptal injections of adrenergic drugs in rats.** *Physiological Psychology*. 4(4):433-438, 1976.

Injections of 5 to 10mg of crystalline norepinephrine into the ventromedial septum of Sprague-Dawley rats decreased the rate of responding and increased the number of shocks received on a free operant avoidance schedule and increased the rate of anticipatory errors and decreased the number of reinforcements received on a differential reinforcement of low rate schedule. Ventromedial septal injections of the alpha-adrenergic receptor blocker, Dibenzylamine, had opposite effects and improved performance on both schedules, whereas intraseptal injections of the beta-adrenergic receptor blockers,

dichloroisoproterenol and dl-4-(2-hydroxy-3-isopropylaminopropoxy)-indole (LB-46), did not modify behavior on these schedules. A different pattern of results was obtained when these drugs were injected into the dorsolateral septum. These results suggest that the septum, especially the ventromedial portion, contains alpha-adrenoceptive neurons that may function to modulate arousal or the effectiveness of both positive and negative reinforcement. 20 references. (Author abstract)

001528 Koob, G.; Del Fiocco, Marina; Iversen, Susan D. Department of Experimental Psychology, Downing Street, Cambridge, England **The behavioural effects of EOS-induced changes in substantia nigra GABA levels.** *British Journal of Pharmacology* (London). 58(3):454P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the behavioral effects of ethanolamine-O-sulfate (EOS) induced changes in substantia nigra GABA levels in rats. Rats were bilaterally injected with EOS in the substantia nigra zona reticulata (SN), and spontaneous locomotor behavior was measured at 30 min intervals up to 72 hrs after injection. Stereotyped behavior was also rated. EOS produced contralateral turning immediately after injection. Stereotyped behaviors including sniffing and biting appeared soon after injection and were still pronounced at 24 hrs. Amphetamine following EOS intensified the ongoing stereotyped behavior both in nature and duration. The results suggest that raising GABA levels in the SN results in heightened functional activity of dopamine containing nigrostriatal tract, producing progressively sensitized spontaneous stereotypy and enhanced motor responses. 2 references.

001529 Kornblith, Carol L.; Hoebel, Bartley G. Department of Psychology, University of North Carolina, Chapel Hill, NC 27514 **A dose-response study of anorectic drug effects on food intake, self-stimulation, and stimulation-escape.** *Pharmacology Biochemistry and Behavior*. 5(2):215-218, 1976.

A comparison was made of the short-term effects in rats of three anorectic drugs (amphetamine, fenfluramine, and phenylpropanolamine) on food intake and responses to obtain brain stimulation and to escape from automatic brain stimulation. At a dose which decreased food intake, amphetamine increased self-stimulation, but not stimulation escape. Fenfluramine decreased both self-stimulation and stimulation escape. Phenylpropanolamine, on the other hand, decreased self-stimulation, but not stimulation escape. Even though all three drugs decreased food intake, each of them had different effects on hypothalamic self-stimulation and escape from stimulation. Only the actions of phenylpropanolamine were in agreement with the hypothesis that lateral hypothalamic reward and aversion reflect the animal's tendency to eat, suggesting that other aspects of reinforcement are also involved in lateral hypothalamic stimulation and were affected differently by these drugs. 25 references. (Author abstract)

001530 Kraemer, Gary W.; McKinney, William T., Jr.; Prange, Arthur J., Jr.; Breese, George R.; McMurray, Teresa M.; Kemnitz, Joseph. Departments of Psychiatry and Psychology, University of Wisconsin Medical School, Madison, WI 53706 **Isoniazid: behavioral and biochemical effects in rhesus monkeys.** *Life Sciences*. 19(1):49-60, 1976.

The possibility that isoniazid, because of its metabolic effects, may produce behavioral effects in monkeys, when administered for prophylaxis against tuberculosis, was investigated. Studies using several behavioral and biochemical dependent variables revealed previously unsuspected effects

attributable to dietary isoniazid in rhesus monkeys. While these effects cannot be classified within any single mode of action, behavioral and pharmacological interactions of the drug suggest that it may act as an antidepressant in this species. Effects on pyridoxal phosphate using enzymes and bodyweight were also demonstrated. These findings identify isoniazid as a possible confounding variable in primate research involving models of human psychopathology, neuroendocrine function, and general physiology. 29 references. (Author abstract modified)

001531 Krimmer, Edward C.; Barry, Herbert, III. School of Pharmacy, Department of Pharmacology, University of Pittsburgh, Pittsburgh, PA 15261 **Discriminative pentobarbital stimulus in rats immediately after intravenous administration.** *European Journal of Pharmacology* (Amsterdam). 38(2):321-327, 1976.

An investigation was carried out to determine whether the discriminative effect obtained within 15 sec after intravenous (iv) infusion of a drug is qualitatively the same stimulus as that which mediates discrimination learning at 5 min or 10 min after intraperitoneal (ip) injection. Rats with chronically implanted venous cannulas were trained to make differential active or passive shock avoidance responses 15 sec after iv administration of pentobarbital or saline. The discriminative pentobarbital stimulus persisted for several min after administration. The pentobarbital response also was elicited in tests at 15 sec after iv injection of chlordiazepoxide or alcohol. Subsequent training at 10 min after ip injection of pentobarbital, followed by tests after ip administration of other drugs, indicated that the discriminative drug stimulus is qualitatively similar with this different route and time interval. A general preference for the passive response over the active response developed only in the second stage of training, during ip injections. 18 references. (Author abstract modified)

001532 Krsiak, M. Institute of Pharmacology, Czechoslovak Academy of Sciences, Albertov 4, 128 00 Praha 2, Czechoslovakia **Effect of ethanol on aggression and timidity in mice.** *Psychopharmacology* (Berlin). 51(1):75-80, 1976.

The effects of ethanol on social behavior of male mice characterized as being aggressive, timid or sociable toward nonaggressive males were investigated. Before ethanol, aggressive mice attacked their partners, timid mice showed defensive/escape activities, and sociable mice intensively investigated their partners. Ethanol exhibited relatively strong aggression stimulating effects in aversively disposed subjects but was not able to suppress timid defensive escape behavior or to stimulate active nonaggressive contacts between strange male mice. 28 references. (Author abstract modified)

001533 Kulig, Beverly M. Department of Physiology, University of Leiden, Wassenaarweg 62, Leiden, The Netherlands **Acute functional tolerance to the motor impairment effects of di-n-propylacetate.** *Pharmacology Biochemistry and Behavior*. 5(5):511-514, 1976.

The effects of di-n-propylacetate (DPA) on treadmill locomotion were studied in rats trained to run treadmill fashion along a moving belt to avoid electric shock. Dose related disturbances in gait and balance were noted as reflected by an increased time off belt. Animals showed a progressive improvement over three trials. A second experiment which measured the effects of DPA either 5 min or 20 min postinjection revealed that the progressive improvement was not due to a diminished drug concentration or to an increased exposure to the drug. It is suggested that acute functional tolerance to the

performance decrement produced by DPA appears to depend upon behavioral processes which enable an animal to overcome a drug induced functional deficit by practicing the task while in the drug state. 15 references. (Author abstract modified)

001534 Kumar, A.; Sharma, H. L.; Sharma, V. N. Department of Pharmacology, S. M. S. Medical College, Jaipur, India **Effect of SAS (a new 10-N-acylaminophenothiazine) on gastric secretion and ulceration in rats.** *British Journal of Pharmacology* (London). 56(4):491-493, 1976.

The antiulcer and antisecretory activity of a new 10-N-acylaminophenothiazine (SAS) was investigated. The drug possesses potent antigastric secretory activity and antiulcer activity in both shay ulcers and stress ulcers. SAS does not exhibit peripheral parasympathetic blocking activity. The pronounced antispasmodic activity of SAS is nonspecific rather than a specific parasympatholytic effect. 14 references. (Author abstract modified).

001535 Lal, H.; Marky, Marguerit; Fielding, S. Department of Pharmacology and Toxicology, University of Rhode Island, Kingston, RI 02881 **Effect of neuroleptic drugs on mouse jumping induced by L-dopa in amphetamine treated mice.** *Neuropharmacology* (Oxford). 15(11):669-671, 1976.

After an injection of amphetamine (4mg/kg) and L-dihydroxyphenylalanine (400mg/kg), a high rate of upward jumping was observed in the treated mice when placed individually in glass jars. Haloperidol, pimozide, chlorpromazine, thioridazine, and clozapine antagonized mouse jumping in a dose dependent manner. promethazine, imipramine, librium, lioresal, nianserin, apomorphine, and aminophyllin were inactive. 11 references. (Author abstract)

001536 Leach, Larry R.; Braun, J. Jay. Arizona State University, Tempe, AZ 85281 **Dissociation of gustatory and weight regulatory responses to quinine following lateral hypothalamic lesions.** *Journal of Comparative and Physiological Psychology*. 90(10):978-985, 1976.

In a two phase experiment, consummatory (Phase 1) and body weight regulation (Phase 2) responses to quinine adulteration of a wet mash diet were measured in rats recovered from bilateral lateral hypothalamic lesions (LH; n=16) and in unoperated control rats (C; n=18). In Phase 1, all rats were fed wet mash adulterated with increasing concentrations of quinine sulfate every other day, and fed unadulterated wet mash on the alternate days. Group LH consumed a significantly lower proportion of quinine adulterated wet mash relative to unadulterated wet mash, displaying a steeper concentration response function and a lower rejection threshold than did Group C. In Phase 2, Groups LH and C were maintained exclusively on quinine-adulterated mash for 20 days. This procedure caused equivalent weight loss in the two groups. Therefore, an apparent exaggerated aversion to quinine adulterated food does not appear to contribute abnormally to the weight regulation exhibited by rats with lateral hypothalamic damage. 11 references. (Author abstract)

001537 Leblanc, A. E.; Kalant, H.; Gibbins, R. J. Department of Pharmacology, University of Toronto, 33 Russell Street, Toronto, Ontario, M5S 2S1, Canada **Acquisition and loss of behaviorally augmented tolerance to ethanol in the rat.** *Psychopharmacology* (Berlin). 48(2):153-158, 1976.

The phenomenon of behavioral augmentation of tolerance (BAT) to ethanol (EtOH) in the rat was replicated in studies

using the moving belt test of intoxication. Rats performing the test daily under the influence of EtOH developed tolerance more rapidly than those receiving the same dose after each daily session on the belt. However, both groups reached the same maximum level of tolerance. Acceleration of tolerance by BAT was proportional to the frequency of performance under the influence of EtOH when total exposure to EtOH was held constant. The degree of tolerance produced by BAT could not be increased by daily gavage with a large dose of EtOH. After termination of EtOH administration, tolerance produced by BAT was lost at the same rate, whether or not daily sessions free of alcohol on the belt test were given. These findings are consistent with the hypothesis that BAT and conventionally produced tolerance differ only in rate. 7 references. (Author abstract)

001538 Leyland, Mark; Robbins, Trevor; Iversen, Susan D. Chemical Defence Establishment, Porton Down, Salisbury, Wilts SP4 0JQ, England **Locomotor activity and exploration: the use of traditional manipulators to dissociate these two behaviors in the rat.** *Animal Learning & Behavior*. 4(3):261-265, 1976.

An apparatus designed by Berlyne was used to dissociate locomotor activity (LA) and inspective exploratory responses in rats with the aid of traditional manipulators. In this apparatus, novel and complex stimulation increased exploration but did not affect LA. Administration of d-amphetamine to the rats increased LA but decreased exploration. These findings provide a double dissociation of the behavioral components. In addition, low intrasubject correlations for the two behaviors were demonstrated. Results are discussed with reference to the need for simultaneous separate measures to obtain valid indices of exploratory behavior and LA. 19 references. (Author abstract modified)

001539 Linseman, Mary Ann. Addiction Research Foundation, Toronto, Ontario M5S 2S1, Canada **Effects of lesions of the caudate nucleus on morphine dependence in the rat.** *Pharmacology Biochemistry and Behavior*. 5(4):465-472, 1976.

The effect of caudate lesions on morphine dependence was studied in morphine dependent lesioned rats, in morphine dependent sham operated controls, in drug naive lesioned animals, and in drug naive sham operated controls. Caudate lesioning failed to suppress naloxone precipitated withdrawal symptoms in the dependent animals. However, the dependent lesioned rats self-administered less morphine than the sham dependent controls. These findings differ from others previously reported. It is hypothesized that the development of processes compensatory to the lesion in animals in this experiment might account for the difference. The results are discussed in relation to possible dissociation of mechanisms governing physical dependence and self-administration. 26 references. (Author abstract modified)

001540 Loew, D. M.; Depoortere, H.; Buerki, H. R. Department of Pharmacology, Biological and Medical Research Division, Sandoz, Ltd., CH-4002 Basel, Switzerland **Effects of dihydrogenated ergot alkaloids on the sleep-wakefulness cycle and on brain biogenic amines in the rat.** *Arzneimittel-Forschung* (Aulendorf). 26(6):1080-1083, 1976.

The effects of four ergot derivatives on the sleep/wakefulness cycle and on brain biogenic amines were studied in male rats. The drugs were dihydroergotoxine, dihydroergonine, dihydroergostine, and dihydro-beta-ergosine. Wistar rats weighing 450 to 550g were fitted with chronically implanted electrodes for EEG and EMG recordings, and were

exposed to a 12 hr light/dark cycle. Biochemical determinations were carried out in RAC rats weighing 120-170 g. Results showed ergot alkaloids, 1 to 30mg/kg i.p., prolonged wakefulness and shortened REM sleep and NEM sleep. 5-hydroxytryptophan had similar effects, except that NREM sleep was not shortened. Norepinephrine content in the brain stem was reduced by 100mg/kg dihydroergotamine, whereas turnover was increased. The same drug at a dose of 10 to 100mg/kg reduced homovanillic acid content in the striatum. At 100mg/kg dihydroergotamine reduced the turnover of serotonin and the 5-hydroxyindoleacetic acid content of whole brain. It is concluded that dihydroergot alkaloids affect both serotonin and dopamine metabolism. 18 references.

001541 Lowe, G. Department of Psychology, University of Hull, Hull, HU6 7RX, England **Haloperidol and light reinforcement in the rat.** *Psychopharmacology* (Berlin). 48(2):233-234, 1976.

The effect of the antipsychotic drug, haloperidol on bar-pressing in the rat was investigated in a light reinforcement situation. Drugged animals responded significantly more for response contingent flickering light and less for steady light than saline injected animals. The finding is consistent with the possible arousal decreasing action of haloperidol and with the notion of an optimum level of arousal. 9 references. (Author abstract)

001542 Lowther, Wayne R.; Isaac, Walter. Department of Psychology, University of Georgia, Athens, GA 30602 **The effects of d-amphetamine and illumination on behaviors of the squirrel monkey.** *Psychopharmacology* (Berlin). 50(3):231-235, 1976.

The effects of d-amphetamine and illumination on behaviors of the squirrel monkey were examined. A behavioral classification and scoring procedure was developed for observing specific responses. The observational procedure along with the photocell method of measuring general activity were then employed to examine the effects of illumination and d-amphetamine on the behavior of squirrel monkeys. It was found that d-amphetamine decreased the incidence of those behaviors seen normally under light conditions while it increased the frequency of behaviors normally seen in the dark. 14 references. (Author abstract)

001543 MacDonald, Ewen. Department of Pharmacology, University of Kuopio, SF-70101 Kuopio 10, Finland **Effect of pyrazole, 4-methylpyrazole, 4-bromopyrazole and 4-iodopyrazole on brain noradrenaline levels of mice and rats.** *Acta Pharmacologica et Toxicologica* (Kobenhavn). 39(5):513-524, 1976.

The effects of pyrazole, 4-methylpyrazole, 4-bromopyrazole and 4-iodopyrazole on brain catecholamine levels, rectal temperature, and exploratory behavior were examined in rats and mice. Four daily doses of pyrazole reduced rat brain noradrenaline (NA) by about 20% when determined 24 hr after the last injection. Neither 4-methylpyrazole nor 4-iodopyrazole had any effect. In mice, only pyrazole caused a dose-dependent decrease in brain NA 24 hr after the last injection; however, both pyrazole and 4-methylpyrazole lowered brain NA when tested 6 hr after a single dose. Acute administration of 4-bromopyrazole and 4-iodopyrazole produced a dose dependent decrease in rectal temperature and exploratory behavior. In high doses, 4-methylpyrazole had similar effects but they did not correlate with the decrease in brain NA. Acute administration of pyrazole had little effect on rectal temperature or exploratory behavior. It is concluded that the NA depleting ef-

fect of pyrazole is not related to inhibition of alcohol dehydrogenase, since other 4-substituted pyrazoles which are more potent inhibitors of the enzyme have little or no effect on brain NA levels. 21 references. (Author abstract modified)

001544 Maj, J.; Kapturkiewicz, Z.; Michaluk, J. Institute for Pharmacology, Polish Academy of Sciences, Ojcowska 52, 31-344 Krakow, Poland /Central action of nomifensine./ *Über die zentrale Wirkung von Nomifensin.* *Arzneimittel-Forschung* (Aulendorf). 26(6):1109-1111, 1976.

Nomifensine, a new antidepressant which strongly inhibits the uptake of dopamine thus leading to dopaminergic stimulation, was studied in male Wistar rats and male Swiss albino mice. Nomifensine in doses of 10 to 20mg/kg stimulated motor activity in rats and mice; low doses of 0.1 to 3mg/kg inhibited motor activity in mice. In mice, nomifensine antagonized the sedation produced by reserpine, alpha-methyltyrosine, FlA-63, phenoxylbenzamine, and reserpine + alpha-methyltyrosine, but did not affect spiroperidol induced sedation. Similar results were obtained in rats, except that nomifensine did not inhibit the results produced by reserpine + alpha-methyltyrosine. Nomifensine, 5 to 20mg/kg, caused dose dependent stereotyping in rats and potentiated amphetamine induced stereotypy. In doses of 10 to 40mg/kg nomifensine antagonized catalepsy induced by spiroperidol, pimozide, fluphenazine, reserpine, alpha-methyltyrosine, pilocarpine, and arecoline, but did not affect the catalepsy produced by a reserpine + alpha-methyltyrosine combination. Nomifensine, 40mg/kg, increased the level of serotonin in rat brain after 1, 2, and 4 hr, and also increased the level of 5-hydroxyindoleacetic acid. Thus, the profile of nomifensine differs from that of the tricyclic drugs, as well as from that of dopaminergic stimulants such as amphetamine and apomorphine. 12 references.

001545 McMillan, D. E.; Leander, J. D. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Interactions between naloxone and narcotic analgesics under three schedules that induce polydipsia.** *Pharmacology Biochemistry and Behavior*. 5(2):195-200, 1976.

The acute effects of several narcotic analgesics on patterns of water consumption under three schedules that induce polydipsia were examined in the rat. Under all three schedules, injections of morphine, methadone, etonitazene, and meperidine generally decreased licking rates and amounts of water consumed, as well as rates of lever pressing under the schedules where lever presses were required. Naloxone almost completely blocked the effects of morphine and etonitazene, but the effects of methadone sometimes were blocked to a lesser degree. Small increases in the rate of licking and amount of water consumed after the lowest dose of meperidine under the schedule requiring lever presses were blocked by naloxone, but the higher doses of meperidine that decreased licking, lever pressing, and amount of water consumed under the three schedules were not blocked by naloxone. It is suggested that there are important differences in the ability of naloxone to antagonize the behavioral effects of different narcotic analgesics. 22 references. (Author abstract modified)

001546 Mollenauer, Sandra; Plotnik, Rod; Southwick, Paula. San Diego State University, San Diego, CA 92182 **Scopolamine: effects on fear or defense responses in the rat.** *Pharmacology Biochemistry and Behavior*. 5(2):157-163, 1976.

The possibility that scopolamine reduces fear responses or defense responses of rats to a cat by blocking olfactory perception of the stimulus cat was investigated. The effects of

scopolamine on defense responses of the hooded rat were also explored further. Rats treated with scopolamine were responsive to olfactory cues from a cat. When cat smell, but not a cat, was present in the apparatus, scopolamine treated rats showed a large and significant suppression of food consumption. The effects of scopolamine on defense responses were shown to be generalizable to an inanimate stimulus, a mechanical robot. Scopolamine caused significantly less freezing and avoidance and significantly shorter latencies to drink in the presence of the robot. It is suggested that scopolamine reduces the defensive response of freezing in a variety of stimulus situations. This finding may have important implications for the literature relating anticholinergic drugs and avoidance behavior. 20 references. (Author abstract modified)

001547 Moller Nielsen, I.; Christensen, A. V.; Hyttel, J. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottilavej 7-9, DK-2500 Copenhagen-Valby, Denmark /Receptor blockade and receptor hypersensitivity after treatment with neuroleptics./ Rezeptorblockade und Rezeptorhypersensibilität nach Behandlung mit Neuroleptika. Arzneimittel-Forschung (Aulendorf). 26(6):1090-1092, 1976.

Receptor blockade, receptor hypersensitivity, and development of tolerance are discussed. In normal mice, methylphenidate causes a stereotyped gnawing syndrome, which is inhibited by major tranquilizers. Apomorphine, on the other hand, does not cause this compulsive gnawing. Mice were given 5mg/kg of the major tranquilizer teflutixol i.p., and the following day were given methylphenidate. On that day and the following day there was complete inhibition of gnawing; thereafter, the effect of the tranquilizer wore off and the mice resumed their compulsive gnawing in response to methylphenidate. The same experiment was repeated using apomorphine instead of methylphenidate. There was no gnawing on the first 2 days, but thereafter intensive gnawing was observed. The gnawing behavior observed on days 3 to 6 after administration of teflutixol followed by methylphenidate can be inhibited by a new dose of teflutixol, but 10 times the dose of the tranquilizer is needed. This happens because the receptor becomes hypersensitive to methylphenidate and apomorphine. After administration of teflutixol, synthesis of catecholamines is accelerated. The antipsychotic effect of major tranquilizers may thus be due not to receptor blockade but rather to receptor hypersensitivity. 2 references.

001548 Morin, L. P.; Powers, J. Bradley; White, Mary. Psychology Department, University of California, Berkeley, CA 94720 Effects of the antiestrogens, MER-25 and CI 628, on rat and hamster lordosis. Hormones and Behavior. 7(3):283-291, 1976.

Results are presented of a study in which antiestrogens were used to test the hypothesis that estrogen exerts a maintenance as well as a priming effect on rat and hamster sexual receptivity as it apparently does for guinea pigs. MER-25 significantly reduced the lordosis quotient (LQ) of ovariectomized female rats when given 2 hours before or 8 hours after estradiol benzoate (EB) injection. MER-25 given at 34 hours (2 hours prior to progesterone) failed to diminish rat LQ. With hamsters, MER-25 in large doses given either at minus 2 hours or 34 hours reduced lordosis duration to 40% of controls, but this effect was confounded by severe illness among the MER-25 injected animals. Lower doses failed to block behavior, but still produced some toxicity. CI 628 greatly reduced hamster lordosis duration and increased lordosis latency when given at 0 hours, but not 34 hours, after EB. The results are consistent with similar previous work on rats and do not support the con-

cept of estrogen maintenance in either rats or hamsters. 21 references. (Author abstract modified)

001549 Mukherjee, B. P.; Pradhan, S. N. Department of Pharmacology, Howard University College of Medicine, Washington, DC 20059 Effects of lithium on foot shock-induced aggressive behavior in rats. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 222(1):125-131, 1976.

The effects of lithium chloride were studied on foot shock induced aggressive behavior categorized as hyperreactivity, preattack, and actual fight or attack scores in rats. The attack score was significantly decreased between 2 hour and 48 hour after administration of all doses tested. Lithium also antagonized amphetamine induced facilitation of the shock induced aggression and scopolamine induced suppression of the shock induced aggression. It is suggested that lithium may act by normalizing induced disturbances of both central adrenergic mechanisms and cholinergic mechanisms, and that the effects may be at least partly responsible for the psychotherapeutic efficacy of lithium as a mood normalizer. 20 references. (Author abstract modified)

001550 Murasaki, Mitsukuni; Hara, Toshio; Oguchi, Toru; Inami, Masaaki; Ikeda, Yukinobu. Dept. of Neuro-Psychiatry, Kitasato University, School of Medicine, Sagami-hara, Japan Action of eniprazole on emotional behavior induced by hypothalamic stimulation in rats and cats. Psychopharmacology (Berlin). 49(3):271-274, 1976.

Action of eniprazole on emotional behavior elicited by hypothalamic stimulation in rats and cats was investigated and comparisons were made with effects of diazepam. Two behavioral patterns were elicited by stimulation of the posteromedial part of the hypothalamus in rats: a food carrying response beginning with exploratory movement and an analog of fear. Eniprazole frequently changed the food carrying response into food taking response and occasionally analogues of fear into food carrying and/or food taking responses. Thresholds for these behaviors were also elevated. Diazepam showed the same effects on the thresholds as eniprazole, having little effect on the behavioral patterns. In cats, eniprazole elevated the thresholds for affective defensive responses induced by hypothalamic stimulation in six of eight cases, but lowered them in two cases. This suggests that eniprazole has a biphasic effect in the CNS. By contrast, diazepam consistently elevated thresholds. Comparing the action of eniprazole with that of diazepam, it can be presumed that the former is a different type of anxiolytic drug than the latter. 15 references. (Author abstract)

001551 Murphy, James M.; Nagy, Z. Michael. Department of Psychology, Bowling Green State University, Bowling Green, OH 43403 Neonatal hyperthyroidism alters the development of behavioral arousal and inhibition in the mouse. Bulletin of the Psychonomic Society. 8(2):121-123, 1976.

The effect of early thyroxine injection on the development of behavioral arousal and inhibition in the mouse was investigated by injecting Ss at 1, 2, and 3 days of age. Ss yielded higher activity levels during the 2nd and 3rd postnatal weeks than saline controls, but no earlier ontogenetic activity peak occurred which could have indicated accelerated development of inhibitory functioning. In experiment 2, however, hyperthyroid mice demonstrated a significant increase in activity following scopolamine injection as early as 15 days of age, whereas controls showed a similar increase at 17 days of age. This finding suggests that neonatal hyperthyroidism results in earlier development of the cholinergic system. 16 references. (Author abstract)

001552 Nakamura, Mitsutaka; Fukushima, Hideaki. Research and Development Center, Pharmaceuticals Division, Sumitomo Chemical Co., Ltd. 4-2-1, Takatsukasa, Takarazuka, Hyogo, 665, Japan **Head twitches induced by benzodiazepines and the role of biogenic amines.** *Psychopharmacology* (Berlin). 49(3):259-261, 1976.

Rats were tested with various benzodiazepines to determine the ability of benzodiazepines to produce head twitches and the relation of the head twitches induced by clonazepam to biogenic amines. Clonazepam induced head twitches in mice in a dose dependent manner and sustained them for at least 120 minutes. Some of the benzodiazepines such as nitrazepam, fludiazepam, and nimetazepam also significantly induced head twitches at doses higher than 10mg/kg, but other benzodiazepines like diazepam, flurazepam, oxazepam, medazepam, and chlorthalidoxepoxide did not significantly induce head twitches at doses up to 60mg/kg. The head twitches induced by clonazepam were more strongly blocked by an antiserotonin drug, cyproheptadine than catecholamine receptor blocking drugs, haloperidol, propranolol, and phentolamine, and were not blocked by gamma-aminobutyric acid (GABA) receptor blocking drugs, bicuculline and picrotoxin, as well as by a glycine receptor blocking drug, strychnine. Clonazepam also increased the head twitches induced by mescaline, a serotonin receptor stimulant. These results indicate that the head twitches induced by clonazepam might be mediated via serotonergic neuron systems. 10 references. (Author abstract modified)

001553 Nakamura, Mitsutaka; Fukushima, Hideaki. Pharmaceuticals Division, Sumitomo Chemical Co., Ltd. 4-2-1, Takatsukasa, Takarazuka, Hyogo 665, Japan **The effect of tricyclic antidepressants and neuroleptics on the peripheral and central action of norepinephrine in reserpine-treated mice.** *European Journal of Pharmacology* (Amsterdam). 38(2):343-348, 1976.

The effect of exogenous norepinephrine on the ptosis induced by reserpine and its modification by tricyclic antidepressants and neuroleptics were studied in reserpine pretreated mice. Subcutaneous injection of norepinephrine and intracerebral injection of norepinephrine reversed the ptosis induced by reserpine in a dose dependent manner. Maximal effects were obtained 15 min after subcutaneous administration and 5 after intracerebral administration. Tricyclic antidepressants min potentiated the effect of norepinephrine but neuroleptics antagonized the effect of norepinephrine. Among tricyclic antidepressants, the potentiating action of secondary amines was stronger than that of tertiary amines. Chlorpromazine blocked the action of norepinephrine more strongly than did the same dose of haloperidol. 26 references. (Author abstract modified)

001554 Natelson, Benjamin H.; Krasnegor, Norman; Holaday, John W. Department of Neurosciences, New Jersey Medical School, 88 Ross Street, East Orange, NJ 07018 **Relations between behavioral arousal and plasma cortisol levels in monkeys performing repeated free-operant avoidance sessions.** *Journal of Comparative and Physiological Psychology*. 90(10):958-969, 1976.

The commonly believed hypothesis that increases in adrenocorticoid levels sensitively reflect behavioral arousal was tested by subjecting monkeys to repeated sessions of free operant avoidance; these sessions produced varying degrees of behavioral arousal over time, which were quantified by a behavioral scoring technique. Cortisol was reliably elevated only in the most aroused subjects early in the first avoidance

session. Although subjects were still aroused later in the session, cortisol had returned to basal levels. During subsequent avoidance sessions, cortisol returned to basal levels and did not increase significantly even when arousal was further manipulated by the superimposition of unavoidable shock during the final avoidance session. The addition of unavoidable shock was associated with a significant correlation between arousal, as reflected by increases in response rate, and magnitude of change, usually decreases, in mean cortisol levels. The frequent occurrence of dissociations between cortisol levels and behavioral arousal, as reflected by behavioral score, operant rate, and shock frequency, indicates that cortisol levels are of little use as a neuroendocrine index of arousal. 31 references. (Author abstract)

001555 Navarro, German; Richardson, Robert; Zuban, Anatole T. Department of Medical Pharmacology and Therapeutics, California College of Medicine, 101 City Drive South, Orange, CA 92668 **Propranolol and morphine.** *Psychopharmacology* (Berlin). 51(1):39-42, 1976.

The effects of propranolol on LD-50's of morphine, morphine induced convulsions, and convulsions induced by electroshock, pentylenetetrazol, or thebaine were studied in mice. The highly specific beta-adrenergic blocking drug sotalol was used as a control drug to determine whether some of the anticonvulsant effects of propranolol could be attributed to beta-adrenergic blockade. Propranolol had no effect on the LD-50 of morphine; however, high doses of propranolol potentiated the convulsant effect of morphine. Overall survival after electroconvulsive shock was similarly modified by propranolol and sotalol; however, only propranolol protected against tonic convulsions. Both propranolol and sotalol protected mice from the tonic phase of pentylenetetrazol induced seizures; however, some propranolol treated animals which developed tonic seizures survived the seizure, while survival in sotalol treated mice occurred only in animals protected against the tonic seizure. Although neither propranolol nor sotalol changed the survival rate in mice receiving convulsant doses of thebaine, propranolol prevented the tonic phase of the convulsive effect. This study does not support the hypothesis that propranolol is a morphine antagonist. It is concluded that propranolol has definite central nervous system effects. 17 references.

001556 Neto, J. Palermo; Carvalho, F. V.; Melito, I. Laboratory of Therapeutics, Faculty of Veterinary Medicine, University of Sao Paulo, Sao Paulo, Brazil **Effects of para-chlorophenylalanine and tryptophan on learning of a brightness discrimination in rats.** *Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 222(2):300-308, 1976.

Both the learning of brightness discrimination, discrimination reversal, and a simple oddity problem, and the pain sensitivity to electric shock were studied in rats. At the end of the last behavioral session all animals were sacrificed, and the levels and rate of 5-hydroxytryptamine (5-HT) synthesis were measured. Para-chlorophenylalanine treatments produced rats which were more effective in coping with a problem; both the levels and turnover rate of brain 5-HT and the pain sensitivity were lower. Results suggest that these differences in learning ability could be a result of the drug's action in pain sensitivity. The possibility that 5-HT might be responsible for these differences is discussed. 28 references. (Author abstract modified)

001557 Numan, Robert; Banerjee, Utpal; Smith, Nelson; Lal, Harbans. Department of Psychology, University of Santa Clara, Santa Clara, CA 95053 **Secondary reinforcement proper-**

ty of a stimulus paired with morphine administration in the rat. *Pharmacology Biochemistry and Behavior*. 5(4):395-399, 1976.

The secondary reinforcement property of a stimulus paired with morphine administration was investigated in pretrained rats. Morphine's effect on resistance to extinction was also investigated. During learning of a maze response by rats, correct responses were reinforced by morphine injection paired with a conditional tone stimulus. During the extinction trials, half of the animals received the tone but no morphine after a correct response; the other half of the animals received neither morphine nor tone. Rats receiving the tone during extinction required significantly more trials to reach extinction criteria than did the controls. In addition, tone presentation during extinction facilitated relearning of the response. The results support the view that morphine is a potent reinforcer, and that stimuli paired with morphine acquire the properties of a secondary reinforcer. 14 references. (Author abstract modified)

001558 Oka, Tetsuo; Hosoya, Eikichi. Department of Pharmacology, School of Medicine, Keio University, Shinjuku-ku, Tokyo 160, Japan **Effect of humoral modulators on morphine-induced increase in locomotor activity of mice.** *Japanese Journal of Pharmacology* (Kyoto). 26(5):615-619, 1976.

The effect of humoral modulators on the morphine induced increase in locomotor activity of mice was studied. The subcutaneous administration of morphine hydrochloride produced a marked increase in locomotor activity in mice. The morphine induced hyperactivity was potentiated by scopolamine and attenuated by physostigmine. In contrast, both methscopolamine and neostigmine, which do not penetrate the blood-brain barrier, had no effect on the hyperactivity produced by morphine. Pretreatment of mice with α -methyltyrosine; an inhibitor of tyrosine hydroxylase, significantly decreased the activity increasing effects of morphine. On the other hand, pretreatment with *p*-chlorophenylalanine, a serotonin depletor, caused no significant change in the hyperactivity. The study suggests that the activity increasing effects of morphine are mediated by the release of catecholamines from adrenergic neurons in the brain. The results are consistent with the hypothesis that morphine acts by retarding the release of acetylcholine at some central cholinergic synapses. It is also suggested from collected evidence that the activity increasing effects of morphine in mice are mediated by mechanisms different from those which mediate the activity increasing effects of morphine in rats. 30 references. (Author abstract)

001559 Palfai, Tibor; Albala, Bruce. Department of Psychology, M-15, Skytop Laboratories, Syracuse University, Syracuse, NY 13210 **Time-dependent performance impairments produced by Metrazol: amnesia or nonspecific drug effect?** *Behavioral Biology*. 17(4):453-461, 1976.

The potential time dependent effect on Metrazol on retention was investigated. Rats maintained on a 23 1/2 hr deprivation schedules were trained to obtain water and were given a convulsive dose of Metrazol following a single trial CER training. Animals which received the drug immediately after the conditioning were amnesic whether they had access to their 30 min home cage water 1 hr or 5 hr following the injection. Animals given the drug 4 hr following training were only amnesic if the home cage watering session followed but not if it preceded the Metrazol injection. The results suggest that the time of home cage water with respect to the amnesic treatment is an important variable in this type of paradigm. They also suggest that the drug produces time dependent memory impairments. 15 references. (Author abstract modified)

001560 Persinger, Michael A.; LaFreniere, Gyslain F.; Falter, Herman. Psychochemistry Laboratory, Dept. of Psychology, Laurentian University, Sudbury, Ontario, Canada **Oral taurine effects on inhibitory behavior: response transients to step-like schedule changes.** *Psychopharmacology* (Berlin). 49(3):249-252, 1976.

Rats were exposed to a behavioral situation that required well learned inhibitory response sequences as well as adjustment to new patterns of inhibition to test the hypothesis that newly acquired behaviors or recent deviations from neuroelectrical homeostasis would be significantly affected by taurine administration, but that older behaviors would not be influenced as much. Rats habituated to differential reinforcement of low rate of responding (DRL) 6-s schedules that required response inhibition in order to obtain reward did not alter their total responses or efficiency ratios (response/reinforcement) when placed orally on 0.9% taurine relative to controls. In three separate experiments, taurine administered rats did show significantly poorer adjustment profiles (higher response/reinforcement ratios) during the 15 min immediately following steplike increases in inhibition time demand to DRL 12-s schedules. The effect was transient and was not significant in subsequent sessions. Taurine rats had been habituated to a DRL schedule intended to induce 'frustration' before the step change did not differ from the taurine group maintained on the normal DRL schedule. No significant differences were noted between taurine and control groups, either before or after taurine administration or before or after the step change in inhibition demand, with respect to defecation in the test chamber, daily fluid consumption, body weight or total responses. It is concluded that oral taurine may inhibit learning during labile periods of adjustment following sudden changes of input demand but does not influence a well learned or established response pattern. These results imply taurine's role in the brain as a 'stabilizer' against short-term input fluctuations. 13 references. (Author abstract modified)

001561 Pieper, W. A. Department of Psychology, Georgia State University, Atlanta, GA 30303 **Great apes and rhesus monkeys as subjects for psychopharmacological studies of stimulants and depressants.** *Federation Proceedings*. 35(11):2254-2257, 1976.

A group of experiments is described in which chimpanzees and orangutans are utilized as subjects in research projects designed to evaluate the effects of stimulant and depressant drugs on learning and performance. Efficiency of performance on a task which measures spaced responding was impaired when subjects smoked cigarettes containing delta9-tetrahydrocannabinol prior to testing. In a sequential learning task, these subjects also demonstrated reduced performance when stimulant drugs (methamphetamine, patermine, phenidmetrazine, d-amphetamine, diethylpropion, benzphetamine), were orally administered before testing. Depressant drugs, (secobarbital, meprobamate, glutethimide, butabarbital), did not produce comparable decrements in sequential learning performance. Physical and behavioral tolerance and dependence on ethanol were investigated in rhesus monkey subjects using a variety of experimental procedures, including forced oral acceptance, intragastric intubation, intravenous infusion, and conditioned voluntary oral acceptance. 12 references. (Author abstract)

001562 Pijnenburg, A. J. J.; Honig, W. M. M.; Struyker Boudier, H. A. J.; Cools, A. R.; van der Heyden, J. A. M.; van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The

Netherlands Further investigations on the effects of ergometrine and other ergot derivatives following injection into the nucleus accumbens of the rat. *Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 222(1):103-115, 1976.

The influence of different pretreatments upon locomotor stimulation induced by injection of ergometrine into the nucleus accumbens of rats was investigated. Phenox-ybenzamine, propranolol, and methysergide produced no clear changes. Reserpine, alone or in combination with alpha-methyltyrosine methylester (alpha-MPT), considerably shortened the delay between injection of ergometrine and start of locomotor stimulation. L-3,4-dihydroxyphenyl-alanine (L-DOPA) but not 5-hydroxytryptophan (5-HTP) clearly antagonized the locomotor stimulation. The effect of ergometrine was strongly diminished following injection of haloperidol directly into the nucleus accumbens. A strong inhibition was also observed following intracerebral administration of (3,4-dihydroxy-phenylamino)-2-imidazoline bromocryptine, LSD, dihydroergotamine and methysergide failed to produce locomotor stimulation following injection into the nucleus accumbens. The results are discussed, especially with regard to the role of dopamine. 33 references. (Author abstract modified)

001563 Plotnik, Rod; Mollenauer, Sandra; Milberg, Leon. San Diego State University, San Diego, CA 92182 **Scopolamine and food-reinforced behavior in the rat.** *Physiological Psychology*. 4(4):443-446, 1976.

A study of the effect of scopolamine on the rate of food reinforced behavior in rats is described. Male hooded rats were food deprived and trained to barpress on a fixed ratio schedule in which every 25th bar press was reinforced (FR25) with liquid food. Three 5 min nonreinforced periods were imposed at the beginning, middle, and end of the session. Under the anticholinergic drug, scopolamine, the rate of barpressing did not differ significantly from control, but there was a significant delay in the onset of barpressing. Scopolamine treated animals did not receive reinforcement until well into the FR25 period. The peripheral control drug, methylscopolamine, did not delay the onset of barpressing. Scopolamine, but not methylscopolamine, caused a change in FR performance: the pauses typical of FR performance were frequently omitted or delayed. Finally, scopolamine, but not methylscopolamine, caused a significant increase in the rate of barpressing during the second and third nonreinforced periods. 12 references. (Author abstract)

001564 Politzer, Ieva R.; McDonald, L. Kathy; Laseter, John L. Department of Biological Sciences, University of New Orleans, Lakefront, New Orleans, LA 70122 **Identification of some volatile endogenous constituents in rat brain tissue and the effects of lithium carbonate and chloral hydrate.** *Research Communications in Chemical Pathology and Pharmacology*. 15(3):469-481, 1976.

Volatile endogenous compounds and volatile compounds in the brain following administration of lithium carbonate and chloral hydrate were assayed by mass spectrometry and gas chromatography in rats. Endogenous volatile compounds present in rat brain tissue were chloroform, a 5-C-aldehyde, dimethyl disulfide, 2,5-dimethyltetrahydrofuran, an 8-C-alkane, xylene, 2-heptanone, heptaldehyde, and 2-n-pentylfuran. Injection of chloral hydrate i.p. led to the appearance of trichloroethanol in rat brain. Lithium carbonate was administered to the rats in their drinking water for the duration of 10 days, increasing dose levels by the 4th day to an average of 14mg/rat. The lithium caused biting and fighting among the rats, but did not induce the production of any new volatile compounds. 16 references. (Author abstract modified)

001565 Posner, Israel; Miley, William M.; Mazzagatti, Nicholas J. Psychology Program, Stockton State College, Pomona, NJ 08239 **Effects of d-amphetamine and pilocarpine on the mouse-killing response of hungry and satiated rats.** *Physiological Psychology*. 4(4):457-460, 1976.

Two experiments which examined some relationships between feeding schedule and two psychoactive drugs on the mouse killing response in rats are described. Experiment 1 showed that the combination of a high dose of d-amphetamine (2.00mg/kg) and food satiation effectively suppresses killing while either factor alone does not. Experiment 2 showed that the combination of a high dose of pilocarpine (30mg/kg) and food deprivation induces a considerable percentage of Sprague-Dawley rats to kill mice while either variable alone does not. Killing and eating mechanisms, therefore, appear to be intricately related in the rat's brain. 17 references. (Author abstract)

001566 Pusakulich, Robert L.; Nielson, Harold C. Psychology and Neurology Services, VA Hospital, Omaha, NE 68105 **Cue use in state-dependent learning.** *Physiological Psychology*. 4(4):421-428, 1976.

Four experiments conducted to determine what cues rats used to escape from a water maze in the normal nondrugged state or while drugged with pentobarbital are described. The subjects were trained to escape from a water maze that either required or enabled them to use place or response cues. The results showed that drugged and nondrugged rats used different cues: drugged rats learned response sequences; nondrugged rats learned either the place of exit from the maze or response sequences. Although some rats selected and used different cues in different states, they showed impaired learning when they were required to use the same cue in both the normal and drugged states. Learning in the drugged state appeared to be different from learning in the normal state, in that drugged rats were restricted in their cue use. The implications of these findings for theories of state-dependent learning are discussed. 17 references. (Author abstract)

001567 Rapp, D. L.; Robbins, T. W. Meldreth Manor, Meldreth, New Royston, Herts SG8 6LG, England **The effects of d-amphetamine on temporal discrimination in the rat.** *Psychopharmacology* (Berlin). 51(1):91-100, 1976.

The effects of dextroamphetamine on performance of a task involving the discrimination between two tones differing only in duration were studied in rats. Dextroamphetamine disrupted performance on the task, although not in an obvious dose related manner. Lever biases were enhanced by the drug, but this effect did not always correlate with deterioration of performance. Dextroamphetamine lengthened both response latency and the performance of terminal components of the operant chain. However, the characteristic pattern of response latencies produced by the two tones was not significantly altered. The results are discussed in terms of whether the drug disrupts discrimination performance by a direct effect on processes of temporal discrimination, or indirectly by its other effects on behavior. 21 references. (Author abstract modified)

001568 Remington, Gary; Anisman, Hymie. Ottawa, Ontario, Canada **Genetic and ontogenetic variations in locomotor activity following treatment with scopolamine or d-amphetamine.** *Developmental Psychobiology*. 9(6):579-585, 1976.

To determine genetic and ontogenetic variations in locomotor activity after treatment with scopolamine or d-

amphetamine, three highly inbred strains of mice (A/J, DBA/2J, and C57BL/6J) were tested in an open field at 14, 21, or 28 days of age. Ten minutes before testing, mice received treatment of saline, scopolamine, or d-amphetamine. The d-amphetamine increased activity in all strains at 14 days and 20 days of age; at 21 days it significantly increased activity in A/J and DBA/2J strains. Increased activity after scopolamine treatment was seen in DBA/2 at 21 days but not in A/J and C57BL/6 until 28 days postnatally. Data suggest a caudal rostral gradient of brain development with the inhibitory cholinergic system developing more slowly than the excitatory catecholamine system. Strain specific differences in activity levels are discussed in relation to the differential rates of cholinergic maturation. 25 references. (Author abstract modified)

001569 Rommelspacher, H.; Bade, P.; Bludau, J.; Strauss, S. Institut für Neuropsychopharmakologie, Freie Universität Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany /Inhibition of monoamine oxidase and day/night rhythm: correlation between physiological and biochemical parameters./ Hemmung der Monoaminoxidase und Tag-Nacht-Rhythmus: Korrelation zwischen physiologischen und biochemischen Parametern. *Arzneimittel-Forschung (Aulendorf)*. 26(6):1078-1080, 1976.

The effect of monoamine oxidase (MAO) inhibitors on motor activity of rats during the light/dark cycle and on the metabolism of serotonin and norepinephrine was studied. Rats were maintained for 10 days on 12 hr of light and 12 hr of darkness and the number of movements over a 15 min period was measured. Pargyline, 20mg/kg s.c. every 2 days, caused a decrease in motor activity both in light and dark, with a rebound effect on the drug free day. During 9 days of treatment MAO activity in the brain decreased to 7% of the control value. Clorgyline, which inhibits only MAO A, caused and increased inhibition of motor activity during the dark phase, with an increase during the light phase. Clorgyline was given 12.5mg/kg s.c. every other day. It is concluded that the rhythmic changes in the levels of serotonin and norepinephrine play a minor role in the circadian rhythm, that MAO inhibitors influence the timing mechanism, and that dopaminergic neurons antagonize activation by adrenergic neurons during the dark period.

001570 Ross, Christopher A.; Trulson, Michael E.; Jacobs, Barry L. Dept. of Psychology, Princeton University, Princeton, NJ 08540 Depletion of brain serotonin following intraventricular 5,7-dihydroxytryptamine fails to disrupt sleep in the rat. *Brain Research (Amsterdam)*. 114(3):517-523, 1976.

Intraventricular administration of 5,7-dihydroxytryptamine (5,7-DHT), which has been shown to selectively affect the serotonin system and which provides an excellent tool for directly examining the relationship between the central nervous system (CNS) serotonin and sleep, was used to test the hypothesis that serotonin is critical for the initiation and maintenance of slow-wave sleep (SWS). Injections of 5,7-DHT, which produce 70% to 90% depletion of forebrain serotonin in the rat, result in only a transient insomnia not significantly different from that observed in control animals. These data challenge the serotonin SWS hypothesis. 34 references.

001571 Ross, Svante B.; Ogren, Sven-Ove. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertälje, Sweden Anti-aggressive action of dopamine-beta-hydroxylase inhibitors in mice. *Journal of Pharmacy and Pharmacology (London)*. 28(7):590-592, 1976.

The effect of two potent dopamine-beta-hydroxylase (DBH) inhibitors on the aggressive behavior of isolated mice and on the aggressiveness produced by L-dopa in normal mice was investigated. Data obtained from administration of 4-methyl-1-homopiperazinedithiocarboxylic acid (FLA 57) and bis(4-methyl-1-homopiperazinylthiocarbonyl)disulfide (FLA 63) showed that the two DBH inhibitors strongly antagonized aggressiveness in isolated mice at doses reducing the noradrenaline concentration in the mouse brain. FLA 63 was more potent than FLA 57, in accordance with the effects on brain noradrenaline. Clonidine, a central noradrenergic receptor agonist, was then administered to determine if it could reverse the blocking effect of FLA 63; Clonidine itself was a potent antagonist of aggressiveness in isolated Ss. It is concluded that aggressive behavior is a complex phenomenon and that results obtained by chemical manipulations must be interpreted cautiously. Suggestions are made for further research. 22 references.

001572 Sanger, D. J.; Blackman, D. E. Department of Psychology, University of Birmingham, P.O. Box 363, Birmingham, B15 2TT, England Effects of diazepam and ripazepam on two measures of adjunctive drinking in rats. *Pharmacology Biochemistry and Behavior*. 5(2):139-142, 1976.

The effects of diazepam and ripazepam on water consumption and on licking as measures of adjunctive drinking were studied in rats. Small doses of diazepam or ripazepam increase the volume of water consumed during an observation session, but the number of licks is not increased to the same extent. Larger doses of diazepam and ripazepam cause decreases both in number of licks and in water intake. Licking may be more sensitive than water intake to the effect of the drugs. It is suggested that the drugs affect the topography of the rats' licking at the water spouts. It is also suggested that in studies of adjunctive drinking measurements of both water intake and number of licks should be obtained. 19 references. (Author abstract modified)

001573 Sanger, D. J.; Blackman, D. E. Department of Psychology, University of Birmingham, P. O. Box 363, Birmingham B15 2TT, England Effects of chlordiazepoxide, ripazepam and d-amphetamine on conditioned acceleration of timing behaviour in rats. *Psychopharmacology (Berlin)*. 48(2):209-215, 1976.

The effects of anxiolytic drugs on conditioned acceleration of operant responding were studied in rats in order to determine whether the effects of these drugs are restricted to suppressive effects on aversive (pre-shock) stimuli. The effects of d-amphetamine were studied for comparison. Chlordiazepoxide and ripazepam increased response rates while decreasing the acceleration of responding produced by the aversive stimulus. Baseline response rates were also increased by amphetamine. At high doses, amphetamine completely abolished the accelerated responding during the preshock stimulus. Although the effects of chlordiazepoxide and ripazepam are consistent with the suggestion that these drugs may attenuate the behavioral effects of aversive stimuli, the similarity of the effects produced by d-amphetamine emphasizes the need for caution in interpreting the effects of anxiolytic drugs on behavior. 36 references. (Author abstract modified)

001574 Sassenrath, E. N.; Chapman, L. F. California Primate Research Center, University of California School of Medicine, Davis, CA 95616 Primate social behavior as a method of analysis of drug action: studies with THC in monkeys. *Federation Proceedings*. 35(11):2238-2244, 1976.

The use of primate social behavior test systems to characterize alteration of central nervous system (CNS) function by lesioning, teletimulation, and psychoactive drugs is discussed. Current observations of effects of acute and long-term chronic administration of delta9-tetrahydrocannabinol in group caged rhesus monkeys are cited to demonstrate the sensitivity and specificity of primate social behavior test systems in characterization of CNS drugs. The time course of drug action proceeds from the acute intoxication stage (sedation, stimulation, decreased social interaction) through behavioral tolerance to the emergence of irritable aggressiveness which is demonstrated in four different social contexts. The influence of social environmental factors and individual differences in social roles on the manifestation of drug effects are discussed. Possible mechanisms of drug on biogenic amines and synaptic receptors compatible with the behavioral data are suggested. 33 references. (Author abstract)

001575 Satinder, K. Paul. Department of Psychology, Lakehead University, Thunder Bay, Ontario P7B 5E1, Canada **Differential effects of morphine on two-way avoidance in selectively bred rat strains.** *Psychopharmacology (Berlin)*. 48(2):235-237, 1976.

Effects of morphine administration were investigated on avoidance behavior in five rat strains. Strain dependent facilitation or suppression of avoidance acquisition was found in animals tested 1 hour after the last administration of morphine. Significant strain differences were found in the incidences of sexual stimulation, diarrhea and wetness, reactivity, and death due to toxicity. 12 references. (Author abstract)

001576 Sayers, A. C.; Burki, H. R. Forschungsinstitut Wander, Postfach 2747, Bern, Switzerland **Influence of anticholinergics and clozapine on the haloperidol induced activation of the dopaminergic system in the striatum of the rat: pharmacologic results.** *Einfluss von Anticholinergika sowie Clozapin auf die durch Haloperidol induzierte Aktivierung des dopaminergen Systems im Striatum der Ratte: Pharmakologische Ergebnisse.* *Arzneimittel-Forschung (Aulendorf)*. 26(6):1092-1093, 1976.

The interaction between haloperidol and anticholinergics was studied in the rat. This is of interest because tardive dyskinesias have been attributed to the development of receptor hypersensitivity following prolonged blocking of dopamine receptors by haloperidol and other major tranquilizers. Atropine, 10mg/kg s.c., or haloperidol, 3mg/kg p.o., or both were given to rats with a unilateral lesion of the striatum, and the effect of these drugs on turning behavior induced by apomorphine was measured. The drugs were given for 6 consecutive days. Atropine alone had no effect, but potentiated the effects of haloperidol on apomorphine induced turning behavior. This correlates with the finding that tardive dyskinesias are more frequent and more severe in patients treated with a combination of a major tranquilizer and an anticholinergic drug. Clozapine, although it is an anticholinergic drug, did not potentiate the effect of haloperidol on turning behavior induced by apomorphine. 11 references.

001577 Schnieden, Harold; Cox, Barry. Department of Pharmacology, Materia Medica and Therapeutics, Stopford Building, University of Manchester, Manchester M13 9PT, England **A comparison between amantadine and bromocriptine using the stereotyped behavior response test (SBR) in the rat.** *European Journal of Pharmacology (Amsterdam)*. 39(1):133-141, 1976.

An investigation was carried out to examine the mechanism of action of bromocriptine. Amantadine, apomorphine and

bromocriptine all produced stereotyped behavior in the rat. Apomorphine was rapid in onset and of short duration, amantadine was slower to reach a maximum, and bromocriptine had a delayed onset and a prolonged action. Amantadine and bromocriptine were antagonized by pimozone suggesting an action on dopamine receptors, and by DL-alpha-methyl-tyrosine suggesting an indirect action. Amantadine, but not bromocriptine, antagonized apomorphine and amantadine also reversed the stereotyped behavior response (SBR) due to bromocriptine. Pretreatment of rats with p-chlorophenylalanine had no effect on bromocriptine. The significance of these results is discussed with references to the proposed mechanism of action of bromocriptine and to the use of multiple drug therapy in parkinsonism. 14 references. (Author abstract modified)

001578 Setler, Paulette; Sarau, Henry; McKenzie, Gerald. Department of Biological Sciences, Smith Kline and French Laboratories, Philadelphia, PA 19101 **Differential attenuation of some effects of haloperidol in rats given scopolamine.** *European Journal of Pharmacology (Amsterdam)*. 39(1):117-126, 1976.

The interaction between haloperidol and scopolamine was investigated in an attempt to clarify the nature and extent of the interaction between cholinergic systems and dopaminergic systems in the brain. The ability of the anticholinergic drug scopolamine to decrease the effectiveness of the neuroleptic haloperidol varied widely. Most severely attenuated was production of catalepsy followed in order of decreasing interference by inhibition of amphetamine induced rotation, inhibition of amphetamine induced stereotyped behavior or apomorphine induced stereotyped behavior, inhibition of conditioned avoidance responding, and, lastly, attenuation of the haloperidol induced increase in striatal homovanillic acid (HVA). By use of a relatively low dose of scopolamine the behavioral effects of haloperidol were dissociated from effects on dopamine turnover in the striatum. If behavioral tests in animals can be related to the clinical effects of neuroleptic drugs, those effects of haloperidol severely reduced by scopolamine may be related to extrapyramidal effects. 24 references. (Author abstract modified)

001579 Silverman, A. P. ICI Ltd., Central Toxicology Laboratory, London, England **Behavioural changes in rats suggesting drug-induced headache.** *British Journal of Pharmacology (London)*. 58(3):439P-440P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed behavioral changes which might indicate headache sequela in rats following administration of nitroglycerin. It is stated that nitroglycerin and other organic nitrates are liable to induce headache in humans after inhalation or skin contact, and may do the same in rats. Such changes are theorized to be manifested by aversion behavior, possibly taste aversion, and an unspecific reduction in spontaneous behavior. Rat pairs were used for this experiment. Treatment of one member of a pair showed no significant change in behavior, but when both members were treated with nitroglycerin there was a significant drop in social approach with little change in nonsocial or escape behavior. Conditioned taste aversion tests showed that treated animals consistently had lower intakes of novel taste fluids than did controls. The effects in both social behavior and conditioned aversion tests were in the predicted direction, but were much smaller than expected. 4 references.

001580 Skinner, Denise M.; Overstreet, David H.; Orbach, Joe. School of Biological Sciences, Flinders University of

South Australia, Bedford Park, South Australia 5042, Australia
Reversal of the memory-disruptive effects of REM sleep deprivation by physostigmine. Behavioral Biology. 18(2):189-198, 1976.

A modified passive avoidance task in rats was used to determine the effects of REM sleep deprivation and the modification of these effects by physostigmine, an anticholinesterase, and scopolamine, an anticholinergic. Three days of REM sleep deprivation before training did not influence the rats' behavior during training, but produced a nearly complete impairment of memory on the retention test three days later. Injections of 0.05mg/kg of physostigmine 20 min after training prevented these memory disruptive effects of REM sleep deprivation. Injections of 0.2mg/kg of physostigmine or 0.5 or 4mg/kg scopolamine did not produce a significant memory improvement in the REM deprived animals, but scopolamine had a memory disruptive effect by itself. These results suggest that the memory disruptive effects of REM sleep deprivation may be mediated in part by their disruption of the cholinergic system. 11 references. (Author abstract)

001581 Smith, D. F. Psychopharmacology Research Unit, Psychiatric Hospital, DK-8240 Risskov, Denmark **Reexamination of vertical activity in rats treated with lithium chloride.** Experientia (Basel). 32(10):1320-1321, 1976.

Johnson's hypothesis that the effect of lithium chloride on vertical rearing in rats is mediated by environmental stimuli was tested in two experiments. In the first study, possible adverse effects of lithium chloride on rearing were examined, and in the second the effects of changed environmental stimuli in lithium treated and control rats were differentially investigated. Lithium was administered i.p. and control rats received similar amounts of distilled water or sodium chloride solution. Results reveal that lithium had several general adverse effects such as licking, prostration, and intestinal irritation. Increased lithium levels were found in rat brain. Results also show that vertical rearing frequencies were significantly lower in lithium treated rats than in controls, regardless of environmental condition. It is concluded that Johnson's hypothesis is invalid and that lithium causes adverse effects independent of, and unrelated to the environment.

001582 Smith, Donald F.; Shimizu, Muneo. Psychopharmacology Research Unit, Psychiatric Hospital, Risskov, Denmark **Effects of alpha methyltyrosine and parachlorophenylalanine on open field behavior in rats given tranlycypromine stereoisomers and lithium carbonate.** Pharmacology Biochemistry and Behavior. 5(5):515-518, 1976.

Parachlorophenylalanine (PCPA) and alpha-methyltyrosine (AMT) were used to study the roles of serotonin and catecholamines in hyperactivity produced by dextrotranlycypromine (d-TC) and levotranlycypromine (l-TC) in rats fed a normal diet (controls) or a diet containing lithium carbonate. Components of locomotor activity were measured in an open field. Lithium decreased ambulation while d-TC increased ambulation and caused jerky side to side movements. PCPA and AMT prevented the effects of d-TC on ambulation but only PCPA prevented the effects of d-TC on movement. The increase in ambulation induced by l-TC was potentiated by PCPA and prevented by AMT. Rearing was increased by both stereoisomers in rats given lithium; this effect was prevented by PCPA and AMT. It is suggested that the roles of serotonergic mechanisms and catecholaminergic mechanisms differ for different components of open field behavior in control rats and in rats given lithium. 24 references. (Author abstract modified)

001583 Smith, Robert. C.; Davis, John M. Texas Research Institute of Mental Science, 1300 Moursund, Texas Medical Center, Houston, TX 77025 **Behavioral evidence for supersensitivity after chronic administration of haloperidol, clozapine, and thioridazine.** Life Sciences (Oxford). 19(5):725-732, 1976.

The effects of chronic treatment with haloperidol, clozapine, and thioridazine in the rat on behavioral indicators of dopaminergic supersensitivity during the withdrawal period is studied. Rats were administered chronic neuroleptics for 6 to 7 weeks. After termination of the chronic drug treatment, the treated animals exhibited greater apomorphine induced stereotyped behavior than the saline controls. Rats treated with thioridazine or clozapine, but not haloperidol, also showed increases in locomotor activity during withdrawal. These findings indicate that behavioral supersensitivity may develop after chronic clozapine treatment as well as after chronic haloperidol. 19 references. (Author abstract modified)

001584 Smits, S. E. Lilly Research Laboratories, Indianapolis, IN 46206 **Antagonism by naloxone of morphine-induced single-dose dependence and antinociception in mice.** Research Communications in Chemical Pathology and Pharmacology. 15(4):689-696, 1976.

The effects of naloxone on the development of morphine-induced single dose dependence and antinociception in mice were investigated. Single dose physical dependence on morphine, as indicated by the mouse withdrawal jumping test, was reduced in a dose related fashion by coadministration of naloxone. In the same dose range, naloxone also antagonized the antinociceptive effect of morphine in the mouse writhing test. The results do not agree with a previous report which indicated that naloxone failed to block acute morphine dependence. (Author abstract modified)

001585 Snider, Stuart R.; Hutt, Cheryl; Stein, Bruce; Prasad, A. L. N.; Fahh, Stanley. Department of Neurology, College of Physicians and Surgeons, Columbia University, 630 West 168th Street, New York, NY 10032 **Correlation of behavioural inhibition or excitation produced by bromocriptine with changes in brain catecholamine turnover.** Journal of Pharmacy and Pharmacology (London). 28(7):563-566, 1976.

The relation between bromocriptine induced changes in brain catecholamine metabolism and two behavioral events, locomotor activity and sympathetic activation was examined in rats. The dopamine agonist, bromocriptine, produced either inhibition or stimulation of motor behavior depending upon the dose and time after administration. Stimulation of motor activity occurred only with high doses after a 1 to 2 h delay. Both inhibition and stimulation were associated with decreased turnover of dopamine in the brain. Release of noradrenaline in brain and noradrenaline plus adrenaline in adrenal varied with motor activity. It is suggested that low doses of bromocriptine inhibit behavior by activating an inhibitory presynaptic receptor, resulting in reduced synthesis and release of dopamine, while high doses cause behavioral excitation by activating the postsynaptic dopamine receptor. 25 references. (Author abstract)

001586 Snyder, E. W.; Beck, E. C.; Dustman, R. E.; Johnson, R. L. no address **Sustained ingestion of methadone and the sleep of monkeys.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 41(6):646, 1976.

At a meeting of the Western EEG Society in San Antonio in February 1976, a report on the effects of sustained ingestion of methadone on sleep were examined over 10 months of

methadone maintenance in monkeys was presented. During the early days of drug induction there was an obvious increase in the frequency of awakening and a decrease in the amount of REM sleep. Even after many months of drug ingestion there was no evidence of systematic tolerance to the sleep disruptive effects of methadone. The results are at variance with preliminary reports of an early tolerance to narcotic sleep disruption.

001587 Sorenson, C. A.; Vayer, J. S.; Goldberg, C. S. Department of Psychology, Amherst College, Amherst, MA **Amphetamine reduction of motor activity in rats after neonatal administration of 6-hydroxydopamine**. *Biological Psychiatry* (Amsterdam). 12(2):133-137, 1976.

The paradoxical decrease in motor activity to amphetamine treatment produced by the administration of 6-hydroxydopamine (6-OHDA) in neonatal rats was studied. The results indicate that 6-OHDA pretreatment, like lead pretreatment, can lead to a reduction in activity after amphetamine administration if the 6-OHDA pretreatment occurs early enough in the postnatal period. The mechanism responsible for this paradoxical response to amphetamine is unclear. The animal treated with 6-OHDA at 1 day of age, like the lead pretreated animal, may serve as a useful animal analog for minimal brain dysfunction (MBD). Clarifying the mechanisms responsible for the paradoxical response to amphetamine might lead to a better understanding of one possible organic etiology of MBD. 13 references.

001588 Sotzing, James H.; Brown, Thomas S. Department of Psychology, DePaul University, 2219 N. Kenmore Ave., Chicago, IL 60614 **Chronic intermittent ethyl alcohol inhalation and avoidance learning**. *Pharmacology Biochemistry and Behavior*. 5(4):417-421, 1976.

The effects of chronic exposure to alcohol using an intermittent inhalation technique which does not cause alcohol dependency on active avoidance learning were studied in rats. The males were impaired on this task but the females were not. Although the males also had reduced body weights, this effect was not responsible for the avoidance impairment. It is concluded that impaired avoidance learning following chronic exposure to alcohol is not specific to dependency models of animal alcoholism. 21 references. (Author abstract modified)

001589 Soubrie, P.; Simon, P.; Boissier, J. J. R. Unite de Neuropsychopharmacologie, INSERM, 2, rue d'Alesia, F-75014 Paris, France **Conditioned suppression: dissociation of learning in baclofen treated rats**. *Experientia* (Basel). 32(10):1323-1324, 1976.

The effects of baclofen, a compound structurally related to gamma-aminobutyric acid (GABA), on conditioned suppression in rats were investigated to elucidate the possible role of a GABAergic mechanism in the amnesic effect of benzodiazepines. Male Wistar rats were administered baclofen and diazepam 30 min before electric shock conditioning or testing trials in which no shock was presented. Shock was used to inhibit drinking behavior. Results reveal that baclofen reduced or suppressed the conditioned avoidance response when given before the shock period and abolished this effect when given before the test period. Baclofen given either prior to testing or prior to training had no effect on the diazepam induced amnesia. It is concluded that the data fail to support a strong relationship between GABA enhanced receptor activity induced by benzodiazepines and their amnesic effect.

001590 Springer, Alan D.; Agranoff, Bernard W. Neuroscience Laboratory, University of Michigan, Ann Arbor, MI 48104 **Puromycin-induced retention deficit in goldfish as a function of attained training performance level**. *Behavioral Biology*. 17(4):547-554, 1976.

To determine whether additional training would prevent the disruption of long-term memory normally induced by puromycin, goldfish received either 20 or 50 active avoidance training trials followed by puromycin (or no treatment) and 10 retraining trials either 1 or 7 days following training. While 50 trials resulted in significantly more training avoidances than 20 trials, the groups which received puromycin showed equivalent retention deficits on Day 7. Comparison of fish whose training performance was high or low further revealed that the degree of the retention deficit was independent of achieved training performance level. These data support the hypothesis that puromycin interferes with a memory fixation process that is initiated only upon completion of the training session. 13 references. (Author abstract modified)

001591 Stalvey, Linda; Daly, John W.; Dismukes, Robert K. National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institutes of Health, Bethesda, MD 20014 **Behavioral activity and accumulation of cyclic AMP in brain slices of strains of mice**. *Life Sciences* (Oxford). 19(12):1845-1850, 1976.

Accumulations of cyclic AMP elicited by norepinephrine, adenosine, and a norepinephrine/theophylline combination were measured in cerebral cortical slices from several inbred mouse strains. There were no apparent correlations between the responses of cyclic AMP generating systems and active avoidance learning for seven strains. Adenosine elicited accumulation of cyclic AMP, and spontaneous behavioral activity did show an inverse correlation in four inbred mouse strains. In individual mice of a randomly bred strain, ability to learn an avoidance task appeared inversely correlated with responsiveness of cortical cyclic AMP generating systems to norepinephrine, but showed no significant correlation with responsiveness to adenosine. 24 references. (Author abstract)

001592 Stanley, M. E.; Glick, S. D. Department of Pharmacology, Mount Sinai School of Medicine of the City University of New York, New York, NY 10029 **Interaction of drug effects with testing procedures in the measurement of catalepsy**. *Neuropharmacology* (Oxford). 15(7):393-394, 1976.

A critical analysis of methods used in investigating drug induced catalepsy in rats is presented. Rats were tested for haloperidol induced catalepsy, using a method described previously by other investigators. The tests were carried out either repeatedly at 10 minute intervals for 2 hours or once at 30 minutes or at 2 hours after drug administration. After either a 2mg/kg or 4mg/kg dose of haloperidol, rats tested repeatedly had catalepsy scores many times greater than those of rats tested once. The results reported by previous investigators are discussed in relation to the current findings. 7 references. (Author abstract modified)

001593 Stern, Judith M.; Mackinnon, Diane A. Department of Psychology, Rutgers University, New Brunswick, NJ 08903 **Postpartum, hormonal, and nonhormonal induction of maternal behavior in rats: effects on T-maze retrieval of pups**. *Hormones and Behavior*. 7(3):305-316, 1976.

The difference in maternal behavior between rats that became maternal after daily pup exposure (sensitization) and those that were primed by endogenous or exogenous hormones

is examined in terms of their pup retrieval behavior in a T-maze extension of the home cage. Postpartum mothers that could not suckle because of prior nipple removal (thelectomy) retrieved as well as, if not better than, intact controls in the T-maze. Hormonal induction of maternal behavior (in 3 days or less) was carried out by hysterectomy ovariectomy estradiol benzoate treatment. The performance of these females was similar to that of the postpartum groups. In contrast, only a small percentage of the sensitized mothers retrieved in the T-maze, whether the latency to onset of their maternal behavior was long (4 to 10 days) or short (3 days or less). It is concluded that hormonal factors associated with pregnancy and/or parturition, but not suckling stimulation, may facilitate T-maze retrieval of pups. The possible ethological significance of the T-maze test as a measure of maternal responsiveness is discussed. 28 references. (Author abstract modified)

001594 Stern, P.; Hukovic, S.; Radivojevic, M. no address /Inhibition of morphine effects by synthetic substance P./ Hemmung von Morphin-Effekten durch synthetische Substanz P. *Experientia* (Basel). 32(10):1326-1327, 1976.

An experimental study was made to determine whether the morphine effect inhibiting action of substance P (SP) and synthetic substance P (SSP) was due to a naloxone effect, or whether the antagonistic action of SSP occurred through another mechanism, independently of the receptor. To test SSP effect on opiate receptors, the method of Manning and Wolf was utilized, based on the principle that the psychomotor unrest evoked by morphine shortens the latency period of pentetrazol seizures. Experiments with mice showed that SSP and naloxone abolished the proconvulsive action of morphine on pentetrazol induced seizures. It is suggested that SP may be a natural antagonist of morphine in the central nervous system.

001595 Stewart, Warren J. Department of Psychology, University of Newcastle, N.S.W., Australia 2308 Effects of undrugged partners on scopolamine-induced changes in activity and sociability. *Psychopharmacology Communications*. 2(2):131-139, 1976.

The effects of scopolamine on frequency of ambulation, rearing, social contacts and distances maintained between animals were investigated in groups of rats in which all animals received the drug and in groups of rats in which only half of the animals received the drug. The presence of non-drugged partners in the groups in which only half of the animals received scopolamine eliminated most of the drug induced changes found in the group in which all animals received scopolamine. It is concluded from this finding that the nature of the social environment affects drug induced changes in activity and sociability. 8 references. (Author abstract modified)

001596 Stewart, Warren; Woods, Pam. University of Newcastle, New South Wales, Australia Assessing interaction's of environment x drug. *Psychological Reports*. 39(2):386, 1976.

In order to assess the effects of scopolamine and environment interaction in two behavioral dimensions, tested rats were exposed to one half of a two chambered box for 30 minutes, removed and then reintroduced to the box with dividing doors removed so that access to the novel half was possible. A relatively low dose of scopolamine was found to reduce ambulation, rearing and preference for the novel half. To test effects of scopolamine on social interaction, a second rat was placed in the box during exposure and test sessions or only during test sessions. It was hypothesized that scopolamine effects on sociability would alter the solitary responses. It was

found that the number of social contacts were not affected by scopolamine, although frequency of contact was higher for rats who had had partners in the exposure and test condition than for rats with partners in only the test condition. The pairing condition produced a nearly significant effect on ambulation; and a significant effect on habituation of rearing, with drugged rats with partners showing a slower rate. 2 references.

001597 Suarez, E. Martin; Barker, Lewis M. Psychology Service, Veteran's Administration Hospital, Waco, TX 76703 Effects of water deprivation and prior LiCl exposure in conditioning taste aversions. *Physiology and Behavior*. 17(4):555-559, 1976.

In a study to assess the effects of water deprivation and prior lithium chloride (LiCl) exposure in conditioning taste aversions, 56 rats were administered extinction tests at 72 hour intervals following treatment with LiCl. Attenuated taste aversion conditioning was observed following preexposure to a LiCl unconditioned stimulus. The amount of fluid consumed during the preconditioning phase was shown to be a factor in the degree of attenuated conditioning. The pharmacological properties of LiCl and the effects of either ad lib or restricted fluid intake in conjunction with state dependent variables were proposed to account for the results. Serum lithium was also assessed in the various groups on conditioning day. The groups did not differ, ruling out an incremental illness hypothesis of attenuated conditioning, which argues that preadministration of a drug leaves the animal mildly ill prior to conditioning. 25 references. (Author abstract modified)

001598 Thornhill, J. A.; Hirst, M.; Gowdey, C. W. Department of Pharmacology, Health Sciences Centre, University of Western Ontario, London, Canada Changes in diurnal temperature and feeding patterns of rats during repeated injections of heroin and withdrawal. *Archives internationales de Pharmacodynamie et de Therapie* (Ghent). 223(1):120-131, 1976.

Changes in the diurnal patterns of body temperature and feeding behavior were monitored in rats before, during, and after a series of daily heroin injections to ascertain whether they are temporally related and if they would reflect the acquisition of tolerance and dependence. Initial heroin injections disrupted diurnal temperature and feeding rhythms; the effects were dose dependent. By the 5th heroin day, hyperthermia and increased feeding occurred in all groups with a shorter latency to onset. Total food intake was higher than on the 1st heroin day, but the diurnal patterns remained disrupted. Changes in both diurnal rhythms again occurred on the 1st withdrawal day as hypothermia, sporadic feeding and hyperirritability were observed. By the 5th withdrawal day, diurnal temperature and feeding rhythms resembled those of the control period. It is concluded that monitoring diurnal temperature and feeding patterns of rats reveals characteristic dose related disruptions after heroin which are modified by repeated doses as tolerance develops and which eventually disappear on withdrawal. 24 references. (Author abstract modified)

001599 Tilson, H. A.; Maisel, A. S.; Jourdan, M. G.; Rech, R. H. Pharmacology Research, Bristol Laboratories, Syracuse, NY 13201 Comparison of the effects of d-amphetamine and lysergic acid diethylamide in two strains of rats having different behavioral baselines. *Behavioral Biology*. 17(4):463-471, 1976.

The rate dependent effects on operant behavior of d-amphetamine and d-lysergic acid diethylamide-25 (LSD) were compared in two different strains of rats. Fisher (F) and Sprague Dawley (SD) rats were trained to press a lever on a

fixed interval (FI) schedule of food reinforcement or to postpone electric footshock on an unsignaled, continuous avoidance schedule. F strain rats responded on the FI schedule at a lower rate than the SD rats. Responding of F rats was increased by low doses of d-amphetamine that had no effect on SD rats. However, linear regression analysis of successive quartiles of FI responding indicated little difference between strains in terms of the rate dependent effects of d-amphetamine. In the continuous avoidance procedure F strain rats had a baseline response rate that was almost twice that of SD rats. However, F strain rats were more sensitive than SD rats to the rate increasing effects of d-amphetamine. Under both schedules of operant responding, SD rats appeared to be more sensitive than F rats to the effects of LSD. Strain related differences in sensitivity to the behavioral effects of d-amphetamine and LSD were not predicted from the observed differences in control baseline. 23 references. (Author abstract modified)

001600 Tseng, Liang-Fu; Brase, David A.; Loh, H. H. Department of Pharmacology, University of California at San Francisco, San Francisco, CA 94143 **Dopaminergic influence on withdrawal jumping behavior in morphine-dependent mice.** Research Communications in Chemical Pathology and Pharmacology. 15(3):435-446, 1976.

Dopaminergic influence on withdrawal jumping behavior was studied in morphine dependent mice. Abrupt withdrawal jumping behavior in morphine dependent mice was accompanied by a decrease in brain dopamine turnover and an increase in brain dopamine level, and was inhibited in a dose dependent manner by apomorphine. Haloperidol did not block naloxone precipitated jumping, but significantly blocked the inhibition by apomorphine. These findings suggest that there may be a decreased dopamine release in the brain during the expression of withdrawal jumping behavior and that dopaminergic activation may be inhibitory to this behavior. 32 references.

001601 Waddington, J. L. Division of Psychiatry, Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England **A behavioural model of the GABA-facilitating action of benzodiazepines: rotational behaviour after unilateral intranigral injection of chlordiazepoxide.** British Journal of Pharmacology (London). 58(3):453P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the rotational behavior of rats following unilateral intranigral injection of chlordiazepoxide as a behavioral model of the GABA facilitated action of benzodiazepines. Male rats were unilaterally injected stereotactically into the substantia nigra zona reticulata (SNR) with chlordiazepoxide. Following recovery only a weak ipsilateral circling/postural deviation was seen. However, pretreatment with amphetamine prior to chlordiazepoxide produced an intense ipsilateral circling that significantly exceeded the mild reactions produced by control procedures. Apomorphine pretreatment produced only weak circling. Injections into the dopamine containing cell bodies of the adjacent substantia nigra zona compacta, both with chlordiazepoxide and saline, produced only mild ipsilateral circling. The results are posited to indicate a facilitatory effect of chlordiazepoxide on GABA transmission in the SNR, and suggest that this model may be useful in the preclinical assessment of benzodiazepines. 4 references.

001602 Waldmeier, P. C.; Maitre, L. Research Department, Pharmaceuticals Division, CIBA-GEIGY Ltd., Basel, Switzerland

land On the relevance of preferential increases of mesolimbic versus striatal dopamine turnover for the prediction of antipsychotic activity of psychotropic drugs. Journal of Neurochemistry (Oxford). 27(2):589-597, 1976.

Drugs possessing (chlorpromazine, haloperidol, clozapine, thioridazine, and sulpiride) or lacking (benzocetamine and perlapine) antipsychotic activity were compared with respect to their ability to enhance alpha-methyl-p-tyrosine induced dopamine disappearance from the mesolimbic area and corpus striatum of rat brain. In addition, their effects on the endogenous concentrations of homovanillic (HVA) and 3,4-dihydroxyphenylacetic (DOPAC) acids in these two brain areas were determined. Some of the drugs enhanced dopamine disappearance in the mesolimbic area more than in the striatum (sulpiride, perlapine, and chlorpromazine). Haloperidol was slightly more active in the striatum than in the mesolimbic area. None of the drugs was more efficient in elevating HVA levels in the mesolimbic area than in the striatum. However, there were large differences in the relative extent of the HVA increases in the two regions. Benzocetamine, perlapine, and chlorpromazine increased HVA concentrations in the mesolimbic area nearly as much as in the striatum. Thioridazine and haloperidol, however, elevated striatal HVA much more effectively. Haloperidol and clozapine increased the DOPAC concentration in both areas to about the same extent. The other drugs were more active in the striatum. The largest difference between both regions was shown by chlorpromazine. Perlapine and benzocetamine, both lacking antipsychotic activity, produced much larger increases of HVA than of DOPAC. This is in contrast to the results obtained with true neuroleptics and may reflect an involvement of release phenomena in the action of these two drugs on dopamine metabolism. These results suggest that a preferential increase of dopamine turnover in the mesolimbic area is not necessarily linked to a better ratio of antipsychotic activity vs extrapyramidal side effects. Moreover, an antiacetylcholine component of dopamine receptor blocking drugs does not seem to be a prerequisite for preferential activity on dopamine turnover in the mesolimbic system. 43 references. (Author abstract modified)

001603 Wallenstein, Martin C. Institute of Neurological Sciences, University of Pennsylvania, Philadelphia, PA 19174 **The effect of nitrous oxide on time estimation in rats.** Bulletin of the Psychonomic Society. 8(2):118-120, 1976.

To determine the effect of nitrous oxide on time estimation in rats and compare it with observed effects on humans, rats were trained on a temporal discrimination task in a two-way shuttlebox while inhaling air and tested while inhaling various concentrations of nitrous oxide. The animals successfully performed the tasks even while inhaling 50% nitrous oxide. At this concentration, response latencies increased. At 20% and 35% nitrous oxide, response latencies decreased. An interaction between conditioned fear in the shuttlebox and the sedative effect of nitrous oxide could explain these results. The ability of the rats to perform successfully a temporal task contrasts with results obtained from human Ss. This could reflect the effect of nitrous oxide on alertness maintained by fear in rats as against different motivations in human subjects. 13 references. (Author abstract)

001604 Way, E. Leong; Iwamoto, E. T.; Khanna, S.; Ho, I. K.; Shen, F.; Loh, H. H. Department of Pharmacology, School of Medicine, University of California, San Francisco, CA **Precipitation of abstinence-like syndrome in morphine-dependent mice by pargyline.** Journal of Pharmacology and Experimental Therapeutics. 199(2):400-407, 1976.

The effects of pargyline in precipitating morphine withdrawal syndrome in morphine dependent mice was studied. Administration of pargyline at 6 hours after withdrawal to morphine dependent mice caused intensified narcotic abstinence behavior, particularly a six fold to nine fold increase in withdrawal jumping response, whereas the effect was unobserved at 1 hour after withdrawal or in animals still receiving morphine. The median effective dose of pargyline required to elicit withdrawal jumping in morphine dependent mice decreased with increasing physical dependence. Additionally, pargyline potentiated naloxone precipitated withdrawal jumping. Administration of other monoamine oxidase inhibitors such as pheniprazine, iproniazid or tranylcypromine failed to alter the incidence of jumping in dependent mice undergoing abrupt morphine withdrawal. Furthermore, dopamine receptor stimulation by amphetamine, pheniprazine or amantadine antagonized the pargyline induced jumping response, suggesting that the increased response is not related to monoamine oxidase inhibition but rather to a possible pargyline induced decrease in dopaminergic activity. 30 references. (Author abstract modified)

001605 Wei, Eddie T. Dept. of Biomedical and Environmental Health Sciences, School of Public Health, University of California, Berkeley, CA 94720 **Chemical stimulants of shaking behaviour.** *Journal of Pharmacy and Pharmacology* (London). 28(9):722-723, 1976.

Evidence is presented here for a novel group of chemicals which have as their predominant effect the ability to stimulate fur coated animals to shake like a wet dog. The pharmacodynamic profile of these agents (haloperidol, perphenazine, morphine sulphate, methadone HCL, clonidine HCL) which cause shaking differs from the recognized groups of behavioral stimulants and may represent a new class of drug action on the nervous system. Research subjects were albino rats, hamsters, guinea pigs, cats, rabbits, dogs, mice, and gerbils. The dose effect relationship was linear over the dosages employed. 12 references.

001606 Weischer, Marie-Luise. Institut für Pharmakologie und Toxikologie der Universität, Westring 12, D-4400 Münster, Germany **A simple device for measuring exploratory activity and motility in mice.** *Eine einfache Versuchsanordnung zur quantitativen Beurteilung von Motilität und Neugierverhalten bei Mäusen.* *Psychopharmacology* (Berlin). 50(3):275-279, 1976.

A simple apparatus of measuring curiosity and motor activity is described. The practicability of the device for testing psychoactive drugs is demonstrated by several experiments in mice. The results show that exploratory behavior or curiosity (looking through holes in the side walls of the experimental cage) is often more influenced by drugs than rearing and motor activity. 12 references. (Author abstract)

001607 Witkin, Jeffrey M.; Barrett, James E. Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27514 **Effects of pentobarbital on punished behavior at different shock intensities.** *Pharmacology Biochemistry and Behavior*. 5(5):535-538, 1976.

The effects of pentobarbital on punished responding was studied in pigeons under conditions where punished behavior: 1) occurred out of the context of a multiple schedule; 2) occurred at more than a near zero rate; and 3) was suppressed by the intermittent presentation of electric shock. Key pecking by two pigeons was maintained initially under a schedule where the first response after 5 min had elapsed produced food. When every 50th response produced a shock, responding

was suppressed. Although rates and patterns of punished responding remained comparable when the shock intensity was reduced by half, pentobarbital produced much greater increases in both overall and local rates of responding at the lower shock intensity. Pentobarbital also produced larger increases in the low rates of responding immediately following shock when the lower intensity shock was in effect. 22 references. (Author abstract modified)

001608 Wuensch, Karl L.; Means, Larry W. East Carolina University, Greenville, NC 27834 **Chlorpromazine reduces avoidance performance deficit in rats with dorsomedial thalamic lesions.** *Bulletin of the Psychonomic Society*. 8(6):439-440, 1976.

Breaking up the freezing response in animals with lesions of the dorsomedial area of the thalamus (DMT) was investigated in a one way active avoidance task by administration of chlorpromazine. Previous studies showed that DMT lesioned rats had a significant performance deficit on acquisition of a one way active shock avoidance task relative to sham operated controls, and administration of amphetamine did not break up the freezing behavior common in lesioned rats upon administration of shock during performance of an avoidance task. In present behavioral testing the DMT lesioned rats were administered intraperitoneal injections of either physiological saline or chlorpromazine in two dose ranges. Results indicate that administration of chlorpromazine prior to testing reduced the performance deficit among the lesioned animals. 14 references. (Author abstract modified)

001609 Yanai, Joseph; Ginsburg, Benson E. Behavioral Genetics Laboratory, Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Long-term effects of early ethanol on predatory behavior in inbred mice.** *Physiological Psychology*. 4(4):409-411, 1976.

A system developed to study the long-lasting neurological and behavioral effects of known amounts of ethanol received transplacentally and via the mother's milk by C57BL/10 and DBA/1 mice offspring is described. The cricket predation behavior of the mice at ages 50 and 51 days was examined. Treated DBA offspring had a 58% reduction in predatory incidences, compared to control, but the already nonpredatory C57 strain was not affected significantly by ethanol. The treated mice that preyed on the crickets had normal latencies. A few general facts on the nature of predatory behavior were also noticed: DBA mice had a higher proportion of predation and shorter latencies than C57; improvement across trials was specific to the C57 strain; there was a high correlation between trials; both sexes displayed predatory behavior; and isolation did not affect predation. It was concluded that predatory behavior offers a simple reliable tool for psychopharmacological research. 20 references. (Author abstract)

001610 Yen-Koo, H. C.; Petersen, Kyle W.; Balazs, T. Food and Drug Administration, Washington, DC **Conditioned avoidance responses in mice surviving a dominant lethal test and in mice treated neonatally with neuroleptic drugs.** *Toxicology and Applied Pharmacology*. 37(1):130, 1976.

The effects of trifluoromazine (TFP) and triethylenemelamine (TEM) on the conditioned avoidance response (CAR) of male survivors of male parents treated with the drugs two weeks (w2), four weeks (w4), or six weeks (w6) before mating were investigated in mice. In addition, the effects of TFP and haloperidol (HPD) on the CAR of mice treated neonatally by subcutaneous injection of the drugs or by administering the drugs to their nursing mothers were stu-

died. No evidence of impairment in learning ability on CAR was detected in survivors from the dominant lethal test with TFP or TEM or in mice treated neonatally with TFP or HPD. 2 references. (Author abstract modified)

001611 Zeller, E. A.; Couper, G. S.; Huprikar, S. V.; Mellow, A. M.; Moody, R. R. Dept. of Biochemistry, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL 60611 **Mescaline: its effects on learning rate and dopamine metabolism in goldfish (*Carassius auratus*)** *Experientia* (Basel). 32(11):1453-1454, 1976.

Pharmacological action of mescaline on goldfish was studied with the Bitterman-Agranoff shock avoidance test. In short-term experiments with high mescaline doses an increase in learning rates was observed. Similar results were obtained with apomorphine and L-dopa. However, when the fish were exposed to smaller mescaline doses (or to fluphenazine) for 3 days, their ability to avoid electric shock was reduced. It was concluded that mescaline induced a release of dopamine which stimulated central dopaminergic symptoms, and subsequently monoamine oxidase destroyed the liberated dopamine. Thus, the ensuing dopamine deficit appears to be responsible for the marked changes in behavior in chronic experiments. 14 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

001612 Bala, S.; Garg, K. N. Pharmacology Department, Medical College, Rohtak, India **Effect of prolonged trifluoperazine, imipramine and haloperidol administration on serum cholesterol: an experimental study in rabbits**. *Pharmacology* (Basel). 14(5):385-389, 1976.

As a result of prolonged intragastric administration of trifluoperazine (TFZ) and imipramine in rabbits, a significant rise in serum cholesterol was observed after 4, 8, and 12 weeks. Haloperidol was ineffective. Hypercholesterolemia produced by TFZ was not associated with increased estriol excretion in urine. Histochemical examination of aorta of TFZ treated animals showed positive "Schultz's reaction" for cholesterol, suggesting a possible causal relationship between TFZ induced hypercholesterolemia and atherogenesis. 18 references. (Author abstract)

001613 Bauer-Moffett, Christina; Altman, Joseph. Laboratory of Developmental Neurobiology, Department of Biological Sciences, Purdue University, West Lafayette, IN 47907 **The effect of ethanol chronically administered to preweanling rats on cerebellar development: a morphological study**. *Brain Research* (Amsterdam). 119(2):249-268, 1976.

The effects of ethanol administered to preweanling rats by vapor inhalation on postnatal body growth, brain growth, and cerebellar growth were investigated. Body growth was not significantly stunted by exposure to ethanol. Arrested brain growth, especially in the cerebellum, appeared shortly after ethanol treatment was begun and persisted into adulthood. Ethanol treatment diminished the growth of both the anterior lobe and posterior lobe and of all layers of the cerebellar vermis. Effects were most pronounced in the anterior lobe and in the medullary layer. Some compensatory growth occurred in the molecular and granular layers during a postweaning rehabilitation period. After 2 days of ethanol treatment the number of Purkinje cells in all 10 vermal lobules was reduced; however, the morphological development of surviving Purkinje cells proceeded normally. The pattern of granule cell neurogenesis in cerebella of ethanol treated did not differ from that of controls, although the ethanol treated animals had con-

sistently fewer cells in all stages of development. A complex age dependent interaction between blood ethanol levels and vulnerable periods in Purkinje cell development is suggested. Mechanisms for the subsequent correlative reduction in the granule cell population are also discussed. 25 references. (Author abstract modified)

001614 Buczko, Włodzimierz. Dept. of Pharmacology, School of Medicine, Michkiewiczza 2, 15-222 Białystok, Poland **The effect of bovine fibrinopeptides on the central action of chlorpromazine and amphetamine in rats**. *Acta Neurobiologiae Experimentalis* (Warszawa). 36(4):447-454, 1976.

A mixture of fibrinopeptides A and B did not evoke any significant central effects in rats when given by intraperitoneal injection, whereas it increased psychomotor activity when injected into a cerebral ventricle. The fibrinopeptides when given by intraperitoneal injection interacted with amphetamine to increase locomotor activity and with chlorpromazine to decrease both locomotor activity and body temperature. It is suggested that the release of fibrinopeptides in various clinical conditions where there is increased fibrinogen fibrin conversion may lead to an altered sensitivity to centrally acting drugs. 13 references. (Author abstract)

001615 Chassaing, C.; Duchene-Marullaz, P. Laboratoire de Pharmacologie Medicale, Faculte de Medecine, F-63001 Clermont-Ferrand, Cedex, France **The influence of meprobamate on heart rate in the conscious dog**. *Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 220(1):45-50, 1976.

The effect of meprobamate on the heartrate was studied in the unanesthetized dog. Mongrel dogs of either sex, weighing 13 to 15 kg were tested. EKG was recorded either by telemetry or by restraining the dog on a table and placing needle electrodes under the skin. Doses of meprobamate ranged from 20 to 50 mg/kg. Some dogs were given 0.2 mg/kg atropine i.v. following the meprobamate. EKG was recorded 2 min after the injections, and then every 5 min for 1 hr. In the telemetric recordings, 50 mg/kg meprobamate caused a statistically significant tachycardia with a peak at 133/min, compared with a peak heartrate in untreated dogs of 83/min. The restrained animals had a control heartrate of 90 to 110/min. Injections of 50 mg/kg meprobamate led to significant tachycardia. Atropine increased heartrate from 91 to 240/min. When injected 30 min after 20 mg/kg meprobamate, atropine increased heartrate from 89 to 244/min; when injected after 50 mg/kg meprobamate, heartrate was increased from 115 to 219/min. The animals frequently fell asleep under the influence of atropine/meprobamate administration. 9 references.

001616 Coniglio, Linda P.; Clemens, Lynwood G. Departments of Biomechanics and Zoology, Michigan State University, East Lansing, MI 48824 **Period of maximal susceptibility to behavioral modification by testosterone in the golden hamster**. *Hormones and Behavior*. 7(3):267-282, 1976.

A study of the effect of neonatal testosterone treatment on adult behavior potential in hamsters is described. Fifty eight male hamsters castrated on the day of birth (day 1) and 80 female hamsters were treated with the free form of testosterone on specific days postnatally. Following androgen treatment in adulthood, animals treated on days 1 and 2 or 3 and 4 postnatally showed significantly higher mounting and intromission frequencies than animals treated later in life. Sexual receptivity measures following ovarian hormone treatment showed no differences among the male groups, while females treated on days 1 and 2 or 3 and 4 were significantly lower in sexual receptivity measures than other females. Histology of

the adult ovaries indicated no modification of normal function. In a subsequent experiment, masculine behavior measures were significantly higher in males treated on days 1 to 10 than in other groups. Among females, masculine behavior was highest in those treated on days 1 to 5. Sexual receptivity in both sexes was depressed by testosterone treatment on days 1 to 10 postnatally, and ovarian histology revealed alterations in gonadal function in females treated on days 1 to 5 and 1 to 10 postnatally. The data suggest that testosterone can be as effective in inducing behavioral masculinization and defeminization as testosterone propionate, provided treatment extends over a prolonged period during early postnatal development. 20 references. (Author abstract modified)

001617 Duggan, A. W.; Hall, J. G.; Headley, P. M. Department of Pharmacology, Australian National University, Canberra, Australia **Morphine, enkephalin, and the substantia gelatinosa**. *Nature*(London). No. 5585:456-458, 1976.

The effects of morphine administered electrophoretically into the substantia gelatinosa (SG) were examined in anesthetized cats. In preliminary experiments, morphine and naloxone were injected electrophoretically into the region of cell bodies. Neurons of spinal laminae IV and V were excited alternately by radiant heat (a noxious stimulus) and by an air jet (nonnoxious stimulus). In these conditions, morphine failed to reduce selectively the activation of cells by either stimulus, and high ejection current produced abnormalities in action potential amplitude and configuration. In contrast, morphine ejected in the SG region caused selective depression of cell responses to the noxious stimulus but not to the non-noxious stimulus. The effect of morphine was reversed by electrophoretic naxoxone in the SG, and by intravenous doses as low as 0.1mg/kg. Of 17 cells tested, enkephalin ejected into the SG reduced the responses of 12 to painful stimuli. With 6 neurons, this reduction occurred without any effect on responses to painless stimuli or on spontaneous firing, but in 5 the predominant effect was a reduction in response to painful stimuli with a smaller reduction in response to painless ones. Recovery from the effects of enkephalin was complete within 10 min after ejection. The reduction of responses to painful stimulation by enkephalin was fully reversed by intravenous naloxone in 5 of 6 cats. Results suggest that a receptor for morphine in the SG is relevant to the reduction by systemic opiates of pain with minimal effects on other sensations. 14 references.

001618 Dutt, J. E.; Mattes, K. D.; Soms, A. P.; Tao, L. C. EM Laboratories, Elmsford, NY **An approximation to the maximum modulus of the trivariate T with a comparison to the exact values**. *Biometrics*. 32(2):465-469, 1976.

A simple approximation to the maximum modulus of the trivariate T with a comparison to the exact values is described. In considering various probability levels for unequal correlations and stated degrees of freedom, the maximum error in the approximate critical values was found to be low. An application in drug toxicity is described to illustrate the technique. 17 references. (Author abstract modified)

001619 Eibergen, Robert D.; Carlson, Kristin R. Department of Psychiatry, Box 3838, Duke University Medical Center, Durham, NC 27710 **Dyskinesias in monkeys: interaction of methamphetamine with prior methadone treatment**. *Pharmacology Biochemistry and Behavior*. 5(2):175-187, 1976.

An investigation was carried out in rhesus monkeys to: 1) determine the effects of chronic methadone treatment on the development of dopamine supersensitivity; 2) evaluate the ef-

fects of emotional stress on monkeys exhibiting oral dyskinesias; 3) determine the effects of methadone, chlorpromazine, or haloperidol on the development of methamphetamine (MA) induced oral dyskinesias; and 4) examine the effects of acute administration of dopaminergic antagonists and other agents on MA elicited stereotyped behaviors. Rhesus monkeys with a history of drinking methadone, but presently drug free, were injected with low doses of MA. They immediately developed oral dyskinesias resembling the symptoms of tardive dyskinesia in humans. Nine of eleven control monkeys failed to develop dyskinesias during prolonged MA administration. A stressful stimulus intensified the MA elicited oral dyskinesias. Control monkeys were then injected with methadone, chlorpromazine, haloperidol, or saline for 45 days. Ten days following this chronic treatment, MA immediately elicited oral dyskinesias in the methadone and chlorpromazine monkeys. Acute administration of the dopaminergic blocking agents chlorpromazine, spiroperidol, and clozapine eliminated MA elicited dyskinesias, whereas the alpha-adrenergic blocker phentolamine was ineffective. Physostigmine blocked the dyskinesias in one of two cases. Sedative doses of phenobarbital and diazepam had no effect on oral dyskinesias. It is suggested that chronic treatment with methadone or other dopamine receptor blocking agents leads to receptor supersensitivity to the actions of MA. 68 references. (Author abstract modified)

001620 Fickentscher, K.; Kohler, F. Pharmazeutisches Institut der Universität Bonn, An der Immenburg, D-5300 Bonn-Endenich, Germany **Teratogenicity and embryotoxicity of some maleinimides**. *Archives of Toxicology* (Berlin). 37(1):15-21, 1976.

The teratogenic and embryotoxic effects of maleinimide, the teratogenic structural central portion of the thalidomide molecule, and five of its derivatives were investigated in mice. According to the electrophilic properties and the spatial requirements of the substituents, the effects were found to be up to 100 times stronger than those of thalidomide and up to 10 times stronger than those of phthalimide. The results are discussed in terms of the distinct electron acceptor behavior of the compounds, which, because of their flat molecular structures, are able to intercalate into the DNA double helix, forming EDA complexes with nucleic acid bases as electron donor molecules. The results are suggested as another possible confirmation of Jonsson's intercalation hypothesis of the thalidomide action. 15 references. (Author abstract modified)

001621 Fitzgerald, T. J. School of Pharmacology, Florida A & M University, Tallahassee, Florida 32307 **Phenobarbital and SKF-525A on vinblastine and vincristine toxicity in mice**. *Experientia* (Basel). 32(5):619-620, 1976.

The effect of the metabolic stimulator, phenobarbital, and the metabolic inhibitor, SKF-525A, on toxicities of two antitumor agents, vinblastine (VLB) and vincristine (VCR), was studied. Six week old DBA/2 male mice were given aqueous solutions of the drug intraperitoneally, one group receiving only VLB or VCR. A second group was treated twice daily with sodium phenobarbital solution for 3 days prior to administration of VLB or VCR. A third group of mice was treated with a single dose of SKF-525A 1 hour before giving VLB or VCR. All deaths occurring within 1 week of drug administration were counted and LD50 values were calculated using a maximum likelihood probit analysis method programmed for digital computation. Pretreatment of animals with phenobarbital increased the LD50 to more than double that of VLB alone, but had considerably less effect on the LD50 of VCR. When

animals were pretreated with SKF-525A a much greater decrease was seen in the LD50 of VLB than in the LD50 of VCR. Results suggest that the lethal toxicity of VLB and VCR in these animals is due primarily to the parent drugs and not to formation of toxic metabolites. 4 references. (Author abstract modified)

001622 Fried, P. A. Department of Psychology, Carleton University, Ottawa, Canada **Short and long-term effects of prenatal cannabis inhalation upon rat offspring.** *Psychopharmacology* (Berlin). 50(3):285-291, 1976.

The short and long-term effects of prenatal cannabis inhalation upon rat offspring were examined. Pregnant rats were exposed to cannabis smoke or smoke from material with cannabinoids removed on days 1-19 of gestation. The number of resorptions was greater in the experimental than the control group. The litter size, length of gestation, sex ratio, live births, and external appearance of the offspring did not differ between the two groups. However, the birth weights of both the male and female offspring of the experimental rats were significantly reduced. Those rats born to control mothers but raised by experimental rats (C-E) were consistently lighter than offspring born and raised by controls (C-C) during the last 15 days of nursing. Those animals born to experimental mothers but raised by controls (E-C) were initially 6-8% lighter than control offspring but by weaning the difference was 3%. Progeny born and raised by experimental mothers (E-E) were consistently lighter than controls during nursing and, even 2 months after weaning, were still significantly smaller. When the offspring were chronically injected with delta9-tetrahydrocannabinol commencing at 100 days of age, the C-E animals developed tolerance sooner than controls, whereas the E-C and, less clearly, the E-E groups took longer to develop tolerance. 33 references. (Author abstract modified)

001623 Friedman, Howard; Carey, Robert J. Syracuse Veterans Administration Hospital, Syracuse, NY **Acute and chronic single dose effects of LSD-25 on visual discrimination in rats.** *Pharmacology Biochemistry and Behavior*. 5(2):223-226, 1976.

The immediate effects and long-term effects of single doses of lysergic acid diethylamide (LSD-25) on visual discrimination performance were studied in rats with preexisting brain damage and in control animals. Rats subjected to either a frontal cortex lesion or to a sham operation were trained to discriminate between lighted and unlit alleys to escape shock. Following intubation with either placebo or LSD-25, they were given discrimination trials 2 hr, 1 week, and 1 month later, but with an increased level of task difficulty. Single dose effects of LSD-25 were observed acutely in a transient impairment of visual discrimination accuracy, and more chronically in slower running time. Although no significant drug/lesion interactions were noted, the results were in the direction of a combinatory effect. The value of increasing the level of posttreatment task was confirmed. 10 references. (Author abstract modified)

001624 Hartmann, Ernest; Zwilling, George. Sleep and Dream Laboratory, Boston State Hospital, Tufts University School of Medicine, Boston, MA 02124 **The effect of alpha and beta adrenergic receptor blockers on sleep in the rat.** *Pharmacology Biochemistry and Behavior*. 5(2):135-138, 1976.

The effects of the beta-adrenergic blocker, propranolol, and the alpha-adrenergic blocker, phenoxybenzamine, on sleep patterns in the rat were examined by means of multiple 8 hr and 24 hr polygraphic recordings. Propranolol had no clear effect on time spent in waking, synchronized sleep, or

desynchronized sleep. Phenoxybenzamine produced a significant increase in desynchronized sleep time and in the number of desynchronized sleep periods. This is consistent with the view that there may be a mechanism inhibiting the onset of desynchronized sleep periods which involves norepinephrine acting at alpha-adrenergic receptors in the brain. 25 references. (Author abstract modified)

001625 Hunt, D. M. School of Biological Sciences, Queen Mary College, University of London, Mile End Road, London E1 4NS, England **A study of copper treatment and tissue copper levels in the murine congenital copper deficiency, mottled.** *Life Sciences* (Oxford). 19(12):1913-1920, 1976.

A study of copper treatment and tissue copper levels in the murine congenital copper deficiency in the mottled mouse is presented. The injection of copper chloride overcomes the lethality and pigment deficiency in the brindled mouse mutant, but copper levels remain depressed in the liver and brain, and a further accumulation occurs in the kidney. The copper dependent synthesis of brain noradrenaline returns to normal, but the activity of brain cytochrome-c oxidase, although increased, remains depressed. Significant changes in tissue copper content of female brindled heterozygotes are reported, and in each case, the changes exceed those expected on the basis of X-inactivation. The significance of these results to the development of a satisfactory treatment regime for this disease in humans is discussed. 14 references. (Author abstract modified)

001626 Karlsen, R. Lund; Fonnum, F. Norwegian Defence Research Establishment, Division for Toxicology, P.O. Box 25, N-2007 Kjeller, Norway **The toxic effect of sodium glutamate on rat retina: changes in putative transmitters and their corresponding enzymes.** *Journal of Neurochemistry* (Oxford). 27(6):1437-1441, 1976.

The effects of sodium glutamate on levels of acetylcholinesterase (AChE), choline acetyltransferase (ChAT), glutamate decarboxylase (GAD), and DOPA decarboxylase in rat retina, superior colliculus, lateral geniculate body, and hippocampus were investigated. Results show that subcutaneous administration of high doses of sodium glutamate to rats during their first week after birth produced an almost total loss of choline acetyltransferase, a 90% reduction in glutamate decarboxylase, and 70% reductions in acetylcholinesterase and DOPA decarboxylase activities in the adult retina. In addition there was a 70% decrease in GABA and 35 to 55% decrease in aspartate, glutamate, glycine, alanine and glutamine. No reduction in taurine was observed. The results support the view that the enzymes are mainly localized in the interneurons of retina and that taurine is present in the photoreceptor cells. Glutamate treatment was also followed by a small reduction in choline acetyltransferase and glutamate decarboxylase of the superior colliculus and in choline acetyltransferase of hippocampus, whereas no changes could be detected in the lateral geniculate body of the adult rat. Unilateral enucleation performed on 1-day-old animals did not alter choline acetyltransferase, acetylcholinesterase, glutamate decarboxylase, and DOPA decarboxylase activities in the superior colliculus and in the lateral geniculate body of the adult rat. 46 references. (Author abstract)

001627 Kinawi, A.; Baumgartl, I. Fachbereich Biologie, WE 03, Freie Universität Berlin, Ostpreussendamm 111, D-1000 Berlin 45, Germany **Studies on the interaction of chlordiazepoxide, diazepam, and nitrazepam with phenprocoumon.** *Untersuchungen zur Interaktion von Chlordiazepoxid,*

Diazepam und Nitrazepam mit Phenprocoumon. Arzneimittel-Forschung (Aulendorf). 26(11):2019-2023, 1976.

Interaction of the benzodiazepine derivatives chlorthalidopexide, diazepam, and nitrazepam, with the anticoagulant phenprocoumon, was studied in rats, noting changes in prothrombin time and changes in concentration of the benzodiazepine or the anticoagulant brought about by the other drug. A single dose of each possible combination between a benzodiazepine derivative and phenprocoumon was given orally. Drug concentrations in serum were measured by high pressure liquid chromatography. All 3 benzodiazepines increased the serum level of phenprocoumon. The benzodiazepines were found to influence the distribution of the anticoagulant by raising phenprocoumon blood level. 45 references.

001628 Kovalev, I. Ye.; Shaydrov, V. V.; Polevaya, O. Yu. Instituta po biologicheskim ispytaniyam khimicheskikh soedineniy Ministerstva meditsinskoy promyshlennosti, Kuznetskaya, USSR /Immunodepressive activity of phenobarbital chemically bound with the protein carrier./ Immunodepressivnaya aktivnost' fenobarbitala, khimicheskii svyazannogo s belkom-nositelem. Farmakologiya i Toksikologiya (Moskva). 6:221-225, 1976.

Experiments with mice immunized with sheep erythrocytes proved that phenobarbital, even in toxic doses, produces no immunodepressive effect. But when it is covalently bonded by the diazo method with a protein carrier, phenobarbital becomes a strong immunodepressant, although not affecting the central nervous system or influencing the immunodepressive activity of cyclophosphamide, an agent metabolically activated in the liver. Free phenobarbital mitigates the effect of cyclophosphamide on the immunological response in mice. 10 references. (Author abstract modified)

001629 Lorez, H. P.; Richards, J. G. Pharmaceutical Research Department, F. Hoffmann-LaRoche and Company Ltd., Basle, Switzerland Effects of intracerebroventricular injection of 5,6-dihydroxytryptamine and 6-hydroxydopamine on supraependymal nerves. Brain Research (Amsterdam). 116(1):165-171, 1976.

Male rats were intracerebroventricularly injected with 5,6-dihydroxytryptamine (5,6-DHT) and 6-hydroxydopamine (6-OHDA) and their brains examined by fluorescence and electron microscopy and the supraependymal nerves examined. From the findings it is concluded that the high toxicity of 5,6-DHT in all supraependymal nerves as compared to 6-OHDA supports the hypothesis of the serotonergic nature of these cells. 22 references.

001630 Matsumoto, M.; Mori, A. Institute for Neurobiology, Okayama University Medical School, Shikata-cho 2-5-1, Okayama, Japan Effects of guanidino compounds on rabbit brain microsomal NA ion-K ion ATPase activity. Journal of Neurochemistry (Oxford). 27(2):635-636, 1976.

An investigation was made of whether convulsions induced by guanidino compounds are associated with an inhibition of rabbit brain microsomal ATPase activity, with specific attention to sodium ion and potassium ion ATPase activity. Effects of the compounds on ATPase were examined by adding each compound to a reaction mixture of brain homogenate, using the following compounds: taurocyamine, glycoyammine, guanidinossuccinic acid, N-acetylarginine, beta-guanidinopropionic acid, gamma-guanidino-beta-hydroxybutyric acid, gamma-guanidinobutyric acid, arginine, homoarginine, guanidine, and methylguanidine. Of these compounds,

only methylguanidine reduced sodium ion/potassium ion ATPase activity to 67% of control values. None of the compounds tested showed any effect on magnesium ion ATPase activity. Methylguanidine behaved as a noncompetitive inhibitor, at a much lower level than that of ouabain. Results suggest that the basic mechanism involved in convulsive effects of guanidino compounds is not connected with brain microsomal sodium ion/potassium ion ATPase activity. 8 references.

001631 Mazur, Mieczyslaw; Szmigielski, Andrzej. Katedra Farmakologii AM, 120a Narutowicza, Lodz 90-145, Poland The effect of prolonged ethanol administration and its withdrawal on catecholamine turnover in the rat brain. Acta Physiologica Polonica (Warszawa). 27(3):281-286, 1976.

Dopamine (DA) and noradrenaline (NA) levels and their turnover were determined in the rat brain after seven weeks of oral administration of ethanol and five or ten days after its withdrawal. No changes in DA and NA levels were found. Elevation of 14C-DA and 14C-NA accumulation and acceleration of 3H-DA disappearance were shown after prolonged ethanol administration. The effect of ethanol on NA turnover was much smaller than that on DA turnover. Five days after ethanol withdrawal no changes were found in DA and NA turnover. Five days later DA turnover was slightly slower than that in the control animals. 17 references. (Author abstract)

001632 Mendell, J. R.; Silverman, L. M.; Verrill, H. L.; Parker, J. M.; Olson, W. H. Division of Neurology, Ohio State University Hospital, Rm. 471, Means Hall, 466 W. Tenth Ave., Columbus, OH 43210 Imipramine-serotonin induced myopathy. Neurology. 26(10):968-974, 1976.

Imipramine and serotonin (5-HT), were used to produce a myopathy in rats. Imipramine was used to simulate a defect in transport of 5-HT observed in the platelets of Duchenne's dystrophy patients. A single series of injections produced focal groups of necrotic and regenerating muscle fibers. In some rats, multiple series of injections resulted in a chronic myopathy with a predilection for proximal muscles, particularly quadriceps. In addition to skeletal muscle lesions, focal areas of myocardial damage were seen. The affected rats had a marked elevation of plasma creatine phosphokinase, serum glutamic oxaloacetic transaminase, and lactic dehydrogenase. Femoral nerve section did not affect the development of muscle lesions. (Author abstract)

001633 Mitchell, Denis; Wells, Claudia; Hoch, Neil; Lind, Karen; Woods, Stephen C.; Mitchell, Linda K. N.I.E.H., P.O. Box 12233, Research Triangle Park, NC 27709 Poison induced pica in rats. Physiology and Behavior. 17(4):691-697, 1976.

Two experiments investigating the effects of poisoning on pica, the consumption of nonnutritive substances, are reported. In the first experiment, 10 naive male rats were poisoned with lithium chloride or Red Squill and offered a choice between food and soil. In a second experiment, 40 naive male rats were poisoned with cyclophosphamide and offered a choice between food and kaolin. Following treatment, poisoned rats in both experiments increased their consumption of the nonnutritive substances. Additionally, rats poisoned with logarithmic doses consumed amounts of the nonnutritive substances proportionate to the amount of poison administered. It is suggested that increased pica is an illness response behavior of the rat, analogous to vomiting in other species, which can be used as an easily quantifiable behavioral assay of noxious drug effects. 37 references. (Author abstract modified)

001634 North, R. Alan; Williams, John T. Neurophysiology Laboratory, Dept. of Pharmacology, Loyola University, Stritch School of Medicine, Maywood, IL 60153 **Enkephalin inhibits firing of myenteric neurones.** *Nature*(London). No. 5585:460-461, 1976.

Previous reports of the endogenous presence of enkephalin in the brain led to an examination of its effects when applied by iontophoresis to units whose activity was extracellularly recorded. An alternative approach was used in which known concentrations of enkephalin were applied to isolated ganglia of the myenteric plexus while recording neuronal activity. Findings are based on recordings from 80 units in 20 guinea pigs. Both methionine/enkephalin and leucine/enkephalin caused an immediate inhibition of neuronal firing; the depression of spike firing was dose related. Firing rates increased immediately upon washing with drug free saline solution. Methionine/enkephalin was approximately 5 times more potent than leucine/enkephalin when tested on the same unit, and 5 to 10 times more potent than morphine or normorphine. Because a tenfold lower concentration of naloxone reversed the action of enkephalin it is suggested that the enkephalin is acting on opiate receptors. Advantages of the technique used in this study over the iontophoretic application of enkephalin *in vivo* are noted. 13 references.

001635 Preache, Maurline M.; Gibson, James E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Effects of cyclophosphamide treatment of newborn mice on the development of swimming and reflex behavior and on adult behavioral performance.** *Developmental Psychobiology*. 9(6):555-567, 1976.

Cyclophosphamide (CP), an antineoplastic agent, was administered subcutaneously to Swiss-Webster mice on the day of birth, and the mice were later tested for developmental or adult behavioral abnormalities. The CP dosages of 20, 30, or 45mg/kg of body weight retarded maturation of swimming ability, and 45mg/kg retarded maturation of the righting reflex. At 7 weeks of age mice treated neonatally with 30 or 45mg/kg of CP had reduced locomotor activity and were more emotionally reactive than controls in an open field. Mice treated with 30 but not 20mg/kg of CP tended to avoid shock less often than controls and those treated with 20mg/kg fell more frequently when crossing a rotating rod for food. Rotorod performance was improved by treatment with 45 but not 30mg/kg of CP. All dosages examined decreased body weight gains but only 30 or 45mg/kg resulted in gross body malformations. The results indicate that CP can functionally impair the development of mice and that some of these impairments are independent of gross body malformations. 29 references. (Author abstract)

001636 Rozonov, Yu. B. Institut farmakologii AMN SSSR, Moscow, USSR **/Cardiovascular effects of diazepam and chlordiazepoxide in experiments with nonanesthetized animals./ Serdechno-sosudistye efekty diazepam i khlordiazepoksida v eksperimentakh na nenarkotizirovannykh zhivotnykh.** *Farmakologiya i Toksikologiya* (Moskva). 6:163-167, 1976.

Experiments with unanesthetized cats showed that symptoms of behavior inhibition in animals following administration of diazepam and chlordiazepoxide are accompanied by hypertension, tachycardia and increased intensity of pressor vasomotor reflexes. Urethan and chlorasole lessened the intensity of the activating effect of the tranquilizers on the central component of the sympathetic nervous tonicity. 13 references. (Author abstract modified)

001637 Rump, S.; Faff, J.; Szymanska, T.; Bak, W.; Borkowska, G. Dept. of Toxicology, Military Institute of Hygiene and Epidemiology, Kozielska 4, P. O. Box 45, 01-163 Warsaw, Poland **Efficacy of repeated pharmacotherapy in experimental acute poisonings with fluostigmine.** *Archives of Toxicology* (Berlin). 35(4):275-280, 1976.

The effectiveness of repeated pharmacotherapy in acute poisonings with fluostigmine was studied in rats. It was demonstrated, that the second *i.p.* administration of obidoxime (40 mg/kg) was without effect. Repeated *i.p.* administration of atropine (10 mg/kg) showed marked efficacy only in animals treated previously with atropine (10 mg/kg) and diazepam (2.5mg/kg). This treatment was without effect in animals treated just after intoxication with atropine (10 mg/kg) and obidoxime (40 mg/kg). Subsequent administration of diazepam (2.5mg/kg) or caramiphen (10mg/kg) was without effect. 8 references. (Journal abstract)

001638 Shellenberger, M. Kent. no address **/Uptake and metabolism of 3-methoxytyramine in the cat brain./** no title. Final report, NIMH Grant MH-21405, 1973. 3 p.

Since 3-methoxytyramine (3-MT) is known to be physiologically active, the accumulation of this compound in drug induced or naturally occurring toxic states may be of importance both experimentally and clinically. The uptake and metabolism of 3-MT was studied in cats both *in vivo* and *in vitro* utilizing 3H-3-MT and these processes were compared to those involving dopamine, the parent neurotransmitter substance, as well as to a reference compound, 14C-urea. The *in vivo* studies indicated that 3-MT is not sequestered by brain tissues although it is rapidly taken into them and metabolized to homovanillic acid and 3-methoxy-4-hydroxy phenylethanol. These metabolites are rapidly cleared from the tissues. *In vitro* studies revealed that 3-MT is not taken up by synaptosomes but it accumulated by striatal and cerebellar slices. The kinetics and characteristics of this process resemble uptake 2 process in the periphery. It is concluded that glial elements are the most likely site of uptake and metabolism of 3-MT but the neuronal perikarya cannot be excluded. (Author abstract)

001639 Shybut, G. T.; Richter, W. R.; Schuster, C. R. Department of Pathology, University of Chicago School of Medicine, 950 East 59th Street, Chicago, IL 60637 **Absence of pathological changes following intravenous methamphetamine and intra-arterial iohalamate meglumine.** *Research Communications in Chemical Pathology and Pharmacology*. 15(1):53-73, 1976.

The relationship between methamphetamine use and severe cerebral vascular lesions was investigated. Eleven Rhesus monkeys received injections of intravenous methamphetamine hydrochloride (Desoxyn) and/or intraarterial 60% iohalamate meglumine (Conray) according to a schedule previously reported to produce marked radiological and pathological changes in the cerebral vasculature of the Rhesus monkey. While radiological changes consistent with impaired cerebral circulation were observed, they could not be correlated directly with the administration of intravenous methamphetamine because of the trauma and variability of the technique utilized. Moreover, significant pathological changes could not be found in animals given intravenous methamphetamine alone, intraarterial iohalamate meglumine alone, or both drugs together. This was true for both drug naive and drug experienced monkeys. It is suggested that radiological changes consistent with decreased cerebral blood flow are not necessarily pathognomonic for reported morphological lesions and that further investigation is required to determine the specific factors necessary to cause the previ-

ously reported changes. 14 references. (Author abstract modified)

001640 Sterman, M. B. Neuropsychology Research, VA Hospital, Sepulveda, CA 91343 **Effects of brain surgery and EEG operant conditioning on seizure latency following monomethylhydrazine intoxication in the cat.** *Biofeedback and Self-Regulation*. 1(3):340, 1976.

In a paper presented at the 1976 Seventh Annual Meeting of the Biofeedback Research Society, Denver, Colorado, results were given of the effects of brain surgery (chronic electrode implantation) and EEG operant conditioning on seizure latency following monomethylhydrazine (MMH) intoxication in the cat. The generalized tonic/clonic seizures elicited by this highly convulsive methyl derivative of hydrazine are unusual because of a characteristic latent period between exposure and seizures. Evidence indicates that the duration of the latent period can reflect seizure susceptibility in relation to the drug, and this concept was used with 30 cats divided into three groups (unoperated Ss, operated Ss with a diversity of electrode placements and experimental treatments, and operated Ss given 3 months of sensorimotor EEG operant conditioning). The EEG pattern rewarded was rhythmic 12Hz to 16Hz activity, termed the sensorimotor rhythm or SMR. Seizure response was measured as the latency, in minutes postinjection, to the onset of generalized tonic/clonic seizures following intraperitoneal administration of 10mg/kg MMH. Operated animals with either no EEG conditioning or noncontingent conditioning showed significantly shorter and more stable seizure latencies than either the unoperated group or the operated group with SMR conditioning. These data indicate that the surgical procedures utilized increased seizure susceptibility in this paradigm, and that SMR operant conditioning countered this effect. The marked variability in seizure latencies noted among unoperated and SMR trained animals suggested individual differences in seizure susceptibility and in response to operant conditioning, respectively. (Author abstract modified)

001641 Szadowaska, Anna; Szmigielska, Helena; Szmigielski, Andrzej. Miedzywydzialowa Katedra Farmakologii AM, 120a Narutowicza, Lodz 90-145, Poland **Turnover of catecholamines in some regions of the rat brain during prolonged vasopressin administration and after its withdrawal.** *Acta Physiologica Polonica* (Warszawa). 27(3):265-268, 1976.

Turnover of noradrenaline (NA) and dopamine (DA) in some regions of the rat brain was determined after 1 and 3 weeks of daily injections of lysine vasopressin (LVP) and 2 weeks after the termination of 28-day LVP injections. Disappearance of 3H-DA was estimated in the hemispheres, brain stem and striatum and of 3H-NA in the hemispheres and brain stem after intraventricular injection of 3H-tyrosine. A significant acceleration of 3H-NA disappearance from the hemispheres was found in all the experimental animals and from the brain stem 3 weeks after LVP administration and 2 weeks after its withdrawal. No marked changes in dopamine turnover in the examined regions of the rat brain were found. Since prolonged vasopressin administration produces hypertension in the rat it seems likely that central NA, but not DA, plays a role in the vasopressin-induced hypertension. 8 references. (Author abstract)

001642 Szmigielska, Helena. Miedzywydzialowa Katedra Farmakologii AM, 120a Narutowicza, Lodz 90-145, Poland **The effect of prolonged vasopressin administration on the level and metabolism of catecholamines in the rat brain and kidneys.** *Acta Physiologica Polonica* (Warszawa). 27(3):259-264, 1976.

Dopamine (DA) and noradrenaline (NA) levels and activities of the enzymes metabolizing catecholamines were determined in the rat brain and kidneys during prolonged (4 weeks) administration of lysine vasopressin (LVP) and 2 weeks after its withdrawal. DA level was elevated during the whole period of experiment. NA level increased mainly after LVP withdrawal. Dopa-decarboxylase activity was elevated in all the experimental animals. Tyrosine and dopamine-beta-hydroxylase activities increased at the final period of LVP administration and after its withdrawal. Activities of MAO and COMT were markedly increased only after 3 weeks of LVP administration. 27 references. (Author abstract)

001643 Walton, K. G.; Baldessarini, R. J. Psychiatric Research Laboratories, Massachusetts General Hospital, Department of Psychiatry, Harvard Medical School, Boston, MA 02114 **Effects of Mn²⁺ ion and other divalent cations on adenylate cyclase activity in rat brain.** *Journal of Neurochemistry* (Oxford). 27(2):557-564, 1976.

The effects of manganese ion and other divalent cations on adenylate cyclase activity in rat brain were studied as related to malfunctions of the central nervous system in animals and man. It is demonstrated that manganese ion caused 8 to 16 fold stimulation of adenylate cyclase activity in homogenates as well as synaptosomes, isolated synaptic membranes, and slices prepared from rat brain. The stimulation occurred at low concentrations of manganese ion, with a doubling of activity at higher concentrations, and was unaffected by a 60 fold excess of magnesium ion. Whether or not magnesium was added, inclusion of a low concentration of manganese reduced, but did not prevent stimulation of adenylate cyclase caused by dopamine in homogenates of corpus striatum. In contrast, calcium ion at a concentration that had little effect on basal cyclase activity completely prevented stimulation by dopamine. The increase of cyclase activity produced by manganese ion in brain homogenates was potentiated by iron. Other ions, notably mercury, lead, copper, and zinc, in order of decreasing potency, inhibited both basal and manganese stimulated cyclase activity. It is proposed that the effect of manganese on adenylate cyclase activity may involve only the catalytic subunit of the enzyme, and that the mechanism is different from that by which either dopamine or iron stimulates the enzyme. These results suggest that the effects of low concentrations of manganese ion and certain other divalent metal ions on adenylate cyclase activity may be involved in their neuropsychiatric or other toxic effects, and that such ions may also participate in normal physiological mechanisms involving cyclic nucleotides. 62 references. (Author abstract modified)

001644 Wright, P. L.; Smith, Sandra H.; Keplinger, M. L.; Calandra, J. C.; Braude, Monique C. Monsanto Company, St. Louis, MO 63166 **Reproductive and teratologic studies with delta9-tetrahydrocannabinol and crude marijuana extract.** *Toxicology and Applied Pharmacology*. 38(2):223-235, 1976.

Synthetic delta9-tetrahydrocannabinol (delta9-THC) and crude marijuana extract (CME) containing 16% delta9-THC were administered in a reproductive performance study in rats and on fetal development in rats and rabbits. Males were dosed from 60 days prior to mating until termination of mating and females were dosed from 14 days prior to mating until 21 days postpartum. Mating and fertility indices were similar for treatment and control groups. No differences between treatment and control groups were seen at an interim sacrifice on gestation Day 14 with respect to corpora lutea, implantation sites, resorption sites, and viable fetuses. The average numbers of pups delivered and viable at birth did not differ

between control and treatment groups, and pup survival was found to be unaffected by treatment. In a perinatal/lactation study, females were dosed from gestation Day 15 until lactation Day 21. No adverse effects of treatment were observed directly or in a cross-fostering study. No evidence of teratogenic activity was obtained for either delta9-THC or CME at delta9-THC equivalent doses on gestation Days 6 to 15 in rats and on gestation Days 6 to 18 in rabbits. Fetal survival and pup survival were found to be reduced at the highest CME treatment level. 17 references. (Author abstract modified)

06 METHODS DEVELOPMENT

001645 Bock, P. R.; Pollock, B.; Schach, S.; Fuchs, A.; Lohaus, R. Department of Pharmacology, Thiemann GmbH, Postfach D-2080, Lunen, Germany **Classification of psychoactive drugs by visually evoked potentials in rabbits by means of multiple discriminant analysis: a possible way of predicting the clinical efficacy of new psychoactive drugs.** *Arzneimittel-Forschung (Aulendorf)*. 26(7):1308-1320, 1976.

The effect of psychoactive drugs on the visually evoked potential in rabbits was studied to learn whether psychoactive drugs could be classified by multiple discriminant analysis. A total of 86 adult male New Zealand albino rabbits, 9 to 12 months old, were used. EEG recordings were made from the caudate nucleus, posterior hypothalamus, mesencephalic reticular formation, intralaminar thalamic nuclei, dorsal hippocampus, amygdala, and visual cortex. Four classes of psychotropic drugs were used: neuroleptics with predominantly antipsychotic effect (haloperidol, fluphenazine), neuroleptics with pronounced sedative and soporific effect (chlorpromazine), antidepressants with predominantly mood brightening effect (imipramine, clomipramine), and antidepressants with sedative effect and neuroleptic component (amitriptyline, doxepine). Using discriminant analysis, the four classes of psychotropic drugs could indeed be put into four groups. Of the three "unknowns" tested, mianserine (GB-94) was allocated to the imipramine group, benzperidol to the haloperidol group, chlorprothixene partly to the amitriptyline group and partly to the chlorpromazine group, and chlorprothixene to the haloperidol group. Findings support the original hypothesis. 68 references.

001646 Brady, Joseph V.; Griffiths, Roland R. Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Behavioral procedures for evaluating the relative abuse potential of CNS drugs in primates.** *Federation Proceedings*. 35(11):2245-2253, 1976.

Behavioral procedures that have been used in the past for evaluating the relative abuse potential of central nervous system (CNS) drugs in primates are reviewed and one of the procedures tested. Studies have focused on performance measurements involving relative rates of drug maintained responding, discrete trial choice determinations, and response cost or progressive ratio values. Relative rate measures have proved historically difficult to use for reliable reinforcement strength determinations. Discrete trial choice procedures for assessing the relative reinforcing properties of stimulus events have recently been reported to effectively discriminate between different drugs and different doses of the same drug. Additionally, response cost or progressive ratio procedures involving systematic increases in the number of responses required for successive drug reinforcements have begun to reveal orderly relationships between different reinforcing drugs at vari-

ous doses and a "breaking point" measure of the relative strength of a reinforcer. Comparisons between selected doses of cocaine, methylphenidate, and secobarbital with a series of five baboons using this procedure have shown that over the same behaviorally active dose range, cocaine breaking points were higher than all of the breaking points obtained with methylphenidate. Dose response differences were also revealed in "breaking point" comparisons between secobarbital on the one hand, and methylphenidate and cocaine, on the other. 25 references. (Author abstract modified)

001647 Grabowski, J.; Sunkin, J. University of Southern California, Schools of Pharmacy and Medicine, Los Angeles, CA 90033 **The "pill popper": a device for drug capsule self-administration by primates.** *Behavior Research Methods & Instrumentation*. 8(6):495-497, 1976.

An apparatus for establishing self-administration of drugs in capsule form by nonhuman primates to investigate the reinforcing properties of behaviorally active drugs is described. The system includes a capsule loading unit combined with a pressurized liquid dispenser and mouth operated drinking tube lever. Operation of the mouth lever results in forced ingestion of a capsule or other solid substance and a measured quantity of liquid. The components of the system are separately programmable and adjustable to permit shaping of pressurized liquid and capsule ingestion through successive approximations. Examination of absorption factors and temporal variables associated with delay of drug reinforcement onset, as well as precision in oral dosage, are thus possible in a model which approximates the most common method and features of drug self-administration in humans. 8 references. (Author abstract modified)

001648 Lockard, Joan S.; Levy, Rene H.; Uhler, Vladimir; Farquhar, John A. Departments of Neurological Surgery and Pharmaceutical Sciences, University of Washington, Seattle, WA 98195 **Interactions of phenytoin and phenobarbital in terms of order and temporal spacing of administration in monkeys.** *Epilepsia*. 17(4):481-485, 1976.

Order and temporal spacing interactions of phenytoin and phenobarbital in terms of plasma levels during multiple dosing in monkeys are investigated. Phenytoin at a dose of 30 mg/kg and phenobarbital at a dose of 3mg/kg were administered separately to four animals (control group) by nasogastric intubation daily for ten days. In four subsequent 10 day periods the drugs were administered together in four other animals (interaction group) at different times of the day (immediately following one another, 1/2 hr apart, and 6 hr apart) and in a different order of administration. Blood samples were obtained on the 5th, 8th, and 10th day of each 10 day period. The plasma data indicated: (a) phenytoin is capable of autoinduction, (b) phenobarbital lowers the levels of phenytoin under the four methods of administration studied here, and (c) phenytoin can affect the levels of phenobarbital. The latter interaction is a function of order and temporal spacing of drug administration. 17 references. (Author abstract modified)

001649 Martin, Parthena; Consroe, Paul. Department of Pharmacology and Toxicology, University of Arizona, Tucson, AZ 85721 **Cannabinoid induced behavioral convulsions in rabbits.** *Science*. 194(4268):965-967, 1976.

Investigations into cannabinoid sensitivity of a particular population of white New Zealand rabbits are reported. Behavioral convulsions were found to occur in this population and inbreeding was undertaken and the resultant offspring tested for sensitivity to delta9-tetrahydrocannabinol. It was

found that low intravenous doses of psychoactive cannabinoids produced convulsions but that the convulsions reduced in severity after long-term administration. Behavioral convulsions were not noted after doses of a number of hallucinogens suggesting that this sensitivity may be specific to cannabinoids. It is concluded that this population of rabbits may provide a potential experimental animal for testing the effects of marihuana, its congeners and its potential antagonists. 12 references.

001650 Nielsen, M. Psychopharmacological Research Laboratory, Department E, Sct. Hans Hospital, DK-4000 Roskilde, Denmark Estimation of noradrenaline and its major metabolites synthesized from 3H-tyrosine in the rat brain. *Journal of Neurochemistry* (Oxford). 27(2):493-500, 1976.

A new procedure is described for the estimation of 3H-labeled noradrenaline (3HNA) and its major metabolites (free and conjugated 3-methoxy-4-hydroxyphenylglycol (MOPEG) and free and conjugated 3,4-dihydroxyphenylglycol (DOPEG)) in the rat brain. The procedure involves adsorption on to alumina, cation exchange chromatography, enzymatic hydrolysis of conjugates, and thin layer chromatography after intraventricular (IVT) or intravenous injection of 3H-tyrosine. In a time course study the formation and accumulation of the metabolites have been measured after IVT injection of 3H-tyrosine. 3H-MOPEG and 3H-DOPEG were found in almost equal amounts during the synthesis phase of 3HNA as well as during the storage and disappearance phase of 3HNA. Maximum levels of conjugated 3H-MOPEG and conjugated 3H-DOPEG were found 2 hours after IVT 3H-tyrosine. The formation of labelled NA metabolites from 3HNA in rat brain in vivo measured as total 3H-MOPEG and 3H-DOPEG sulfate ester was influenced by drugs affecting 3HNA synthesis, release, and metabolism. Results following drug treatment support the validity of the method and provide in addition confirmation of the specificity, since both the level of catecholamines and total metabolites can be varied independently. 41 references. (Author abstract modified)

001651 Shah, B. K. Rockland Research Institute, Orangeburg, NY 10962 Data analysis problems in the area of pharmacokinetics research. *Biometrics*. 32(1):145-157, 1976.

A few pertinent papers in the field of pharmacokinetics are reviewed, and five topics in data analysis problems in the area of pharmacokinetics research are discussed: 1) assumption of first order rate constants; 2) the question of unique solution of kinetic parameters in linear compartment models; 3) the question of unique solution of kinetic parameters in nonlinear compartment models; 4) equations for multiple doses in a multicompartment situation; and 5) statistical considerations in multicompartment models. Data taken from Wagner's experiment are used to illustrate the methodology of compartment analysis. It is noted that from the data pertaining to only one compartment, it is not always possible to estimate all the first order rate parameters of linear and non linear compartment systems. When multiple varying doses are administered at different intervals of time, the equations quantifying the maximum and minimum amount of drug accumulated in each interval may be used. To obtain estimates of kinetic parameters, statistical adjustments may be used in the kinetic equations. 15 references. (Author abstract modified)

001652 Wielosz, M.; de Gaetano, G.; Garattini, S. Lab. for Haemostasis and Thrombosis Research, Istituto de Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62, I-20157 Milan, Italy Improved method for evaluating the inhibition of (14C)5-

hydroxytryptamine uptake by rat platelets. *Journal of Pharmacy and Pharmacology* (London). 28(9):717-718, 1976.

An improved method for evaluating the inhibition of 14C-5-hydroxytryptamine (5-HT) uptake by rat platelets is presented. Using low substrate concentrations and short incubation times, 14C-5-hydroxytryptamine uptake in rabbit platelets was found to be more comparable to that occurring in rat synaptosomes. This finding is considered to lend further support to the usefulness of platelets as a model for the study of serotonergic nerve endings. The possibility of further improving the methodology for measuring 5-HT uptake by platelets and its pharmacological inhibition is noted. 12 references.

CLINICAL PSYCOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

001653 Abt, K.; Baumann, U.; Debus, G.; Ferner, U.; Heimann, H.; Muller-Oerlinghausen, B.; Woggon, B. no address /Clinical trials: methodology versus practice -- attempt at a compromise./ *Klinische Prüfungen: Methodik versus Praxis -- Versuch eines Kompromisses.* *Arzneimittel-Forschung (Aulendorf)*. 26(6):1025-1026, 1976.

The methodology of clinical trials was discussed in a workshop in which the seven authors were participants. The related factors involved in a drug trial are: 1) the drug itself (dose, duration of action, side-effects, drug/drug interactions); 2) the patient (expression of symptoms, personality, life situation); 3) the course of illness (length of illness, spontaneous remissions); 4) the clinic (open or closed ward, occupational therapy, relations between patients and nursing staff, ambulatory treatment); and 5) the study itself (expectations of investigators, and length of study). Rating systems and tests are discussed, followed by a short discussion of statistics. The importance of interdisciplinary communication is stressed. 13 references.

001654 Binder, H.; Gerstenbrand, F.; Grunberger, J.; Grundig, E.; Schubert, H. Neurologische Universitätsklinik, Lazarettgasse 14, A-1097 Vienna, Austria /Experience with an L-dopa retard preparation in peroral long-term therapy of Parkinson syndrome./ *Erfahrungen mit einem L-Dopa-Retard-Präparat in der peroralen Langzeittherapie des Parkinson-Syndroms.* *Nervenarzt (Berlin)*. 47(11):656-660, 1976.

Clinical trial was made of a new L-dopa retard preparation in 50 patients with Parkinson syndrome of varied etiology. Therapeutic short-term and long-term effects were measured by clinical observation, rating procedures, psychodiagnostic test battery, and measurement of L-dopa and amino acid levels in the blood. The spectrum of action and onset of effect of the retard preparation were found to correspond to that of a normal levodopa compound. The advantage of the retard mode is that the daily dose may be reduced, with an accompanying substantial reduction in side-effects, and regular, high blood serum levels. 8 references. (Author abstract modified)

001655 Bobon, J.; Parent, M.; Toussaint, C.; Pinchard, A. Clinique psychiatrique universitaire, Rue Saint-Laurent 58, B-4000 Liege, Belgium /Long-acting neuroleptics: a preliminary study of clopimozide (R29764)./ *Neuroleptiques a longue durée d'action. IV. Etude préliminaire du clopimozide (R 29764).* *Acta Psychiatrica Belgica (Bruxelles)*. 76(1):138-148, 1976.

To evaluate the efficacy and toxicity of the neuroleptic, clopimozide (R-29764), a preliminary study was made on 10 hospitalized patients consisting of nine schizophrenics and one neurotic with a depressive paranoid character, average age 36 years. It was found that clopimozide's action is mainly ataraxic but also antidelusional, long acting and accompanied with minimal side-effects. It is particularly indicated in the maintenance therapy of psychotics at a weekly dosage of 7.5 to 25mg. The present conclusions are preliminary because of the limited number of patients and the rigidity of the trial protocol suggested. Brief case histories of the subjects are included. 5 references. (Author abstract modified)

001656 Chou, Feng-te; Khan, A. Hameed; Driscoll, John S. Drug Research and Development Program, Division of Cancer

Treatment, National Cancer Institute, NIH, Bethesda, MD 20014 Potential central nervous system antitumor agents. Aziridinylbenzoquinones. 2. *Journal of Medicinal Chemistry*. 19(11):1302-1308, 1976.

A series of 15 2,5-diaziridinyl-3,6-bis(alkylamino)-1,4-benzoquinone derivatives was synthesized and evaluated as central nervous system antitumor agents in the murine intracerebral and ependymoblastoma brain tumor systems. Intraperitoneal activity was evaluated in the leukemia, and melanocarcinoma tumor models. The more hydrophilic hydroxyalkylamino compounds were the most effective in the intraperitoneal ascites systems with the dihydroxypropylamino and hydroxyethylamino analogues producing long-term survivors. The simple, more lipophilic monoalkylamino and dialkylamino derivatives were most effective in the intracerebral systems. Multiple long-term survivors were obtained with the methyl, ethyl, and dimethylamino compounds in the ependymoblastoma brain tumor system. The parent amino analogue 12 was very active in several tumor models. The relationships between structure, activity, and water solubility are discussed. 52 references. (Author abstract)

001657 Clarke, Coral H.; Nicholson, A. N.; Stone, Barbara M. Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire, England /Effect of the 1,5-benzodiazepines, clobazam and triflubazam, on the sleep of man. *British Journal of Pharmacology (London)*. 58(3):439P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed the effect of the 1,5-benzodiazepines, clobazam and triflubazam, on sleep in man to assess their usefulness as hypnotics offering less potential for impairing performance in skilled activity the next day. Six healthy male volunteers were used. Neither drug showed any significant change in total sleep time or in duration of each sleep stage, but clobazam reduced sleep onset latency and latency to stage 3. There was also some evidence of reduced awakenings to stage 0 and stage 1 activity. Triflubazam did not change latencies to sleep stages, but there was some evidence of reduced awakenings to stage 0 and 1 activity. 2 references.

001658 Darcourt, Guy. Service de Psychiatrie et de Psychologie Médicale, Hôpital Pasteur, F-06031 Nice Cedex, France /Comparison of lithium salts./ *Comparaison entre les différents sels de lithium.* *Evolution Psychiatrique (Toulouse)*. 41(3):595-610, 1976.

Different properties of lithium, including intestinal absorption, therapeutic efficiency, and side-effects are studied. Charts of physical chemical properties of lithium salts including carbonate, gluconate, sulfate, chloride, acetate, citrate, disuccinate, glutamate, and oxalate are given. Human and animal intestinal absorption of lithium are compared and lithium stability is examined. Side-effects, including biological and digestive tolerance, toxicity, and weight gain, are discussed. Results of a study of the use of sulfates and carbonates to slow down absorption rate are stated to be inconclusive. In conclusion, more studies of lithium are needed. 33 references.

001659 Debus, G.; Aufdembrinke, B. Psychologisches Institut der Universität Düsseldorf, Universitätsstrasse 1, D-4000 Düsseldorf, Germany /Comparison of experimental psychological

and clinical findings on the effect of a test drug./ Vergleich experimentalpsychologischer und klinischer Befunde zur Wirkung einer Prüfsubstanz. Arzneimittel-Forschung (Aulendorf). 26(6):1141-1145, 1976.

Bay-g-5653, a thienodiazepine under investigation, was compared with diazepam among neurotic and psychosomatic patients and 180 healthy male students. The patient group included 45 outpatients and 120 inpatients. Daily dosages were 15 or 30mg Bay-g-5653 and 15mg diazepam, and the length of treatment was 3 weeks. Students were given a single dose of either 2.5, 5, or 10mg Bay-g-5653, 5mg diazepam, or placebo. Emotionally stable students showed lessening of activation under 10mg Bay-g-5653 and diazepam, and an improvement in general comfort under 2.5mg Bay-g-5653. Emotionally labile students showed no significant difference between placebo and the active drugs, although there was a tendency toward increased general comfort under diazepam. Both inpatients and outpatients showed improvement under all three drug regimens, but improvement was greater among the outpatients. Inpatients seemed to do a little better on Bay-g-5653 than on diazepam, but there was no difference between drugs among the outpatients. 5 references.

001660 Ehsanullah, R. S. B. no address **Tandamine: a new antidepressant.** British Journal of Clinical Pharmacology (London). No. 3:950P, 1976.

A double-blind placebo controlled study of tandamine, a new thiopyranoidole derivative antidepressant, was undertaken in depressed subjects who were given 50mg single oral doses of tandamine or desipramine. Results reveal that tandamine possessed significant anticholinergic activity, reduced appetite, and produced sedation 2 to 6 hours after ingestion. Tandamine also proved to be a more potent inhibitor of tyramine pressor responses than desipramine. It caused a 25% inhibition of 5-hydroxytryptamine (serotonin) uptake and a 30% inhibition of dopamine uptake into blood platelets in vitro. Plasma levels of tandamine varied between 18 and 89microgram/ml 3 to 4 hours after oral administration. (Journal abstract modified)

001661 Fujiwara, J.; Ishino, H.; Baba, O.; Hanaoka, M.; Sasaki, K.; Otsuki, S. Department of Neuropsychiatry, Okayama University Medical School, Okayama, Japan **Effect of flupenthixol on depression with special reference to combination use with tricyclic antidepressants: an uncontrolled pilot study with 45 patients.** Acta Psychiatrica Scandinavica (Kobenhavn). 54(2):99-105, 1976.

In an open, uncontrolled trial flupenthixol (a thioxanthene derivative) was administered to 45 patients with endogenous depression. In 36 patients flupenthixol was used in combination with previously administered tricyclic antidepressants, and in nine patients it was used alone. Clinical effect was apparent within one week in 63% of the subjects and within two weeks in 93%. The drug was markedly effective in eight patients, effective in nine, fairly effective in 12, and ineffective or aggravating in 16. Four patients showed transient manic symptoms. Side effects, including insomnia and slight extrapyramidal symptoms, occurred in 13 patients. Sedative and/or hypnogenic effects were rare. Flupenthixol's effect on psychomotor retardation was striking, and other clear benefits were relief of depressive mood, psychic anxiety, and agitation. It is recommended that the drug be given, as supplementary medication, to patients whose depressive symptoms other than psychomotor retardation have already improved with current tricyclic antidepressants and in whom, before antidepressant medication, psychomotor retardation was a major feature. 7 references. (Author abstract modified)

001662 Gilbert, Malcolm S.; Hanover, Rita M.; Moylan, David S.; Caruso, Frank S. Department of Anesthesiology, St. Joseph's Hospital Health Center, and Medical Department, Bristol Laboratories, Syracuse, NY **Intramuscular butorphanol and meperidine in postoperative pain.** Clinical Pharmacology and Therapeutics. 20(3):359-364, 1976.

Based upon evidence that butorphanol is approximately equivalent to nalorphine as a narcotic antagonist, butorphanol, 1, 2, and 4mg/70kg, and meperidine, 40 and 80mg/70kg, were compared for analgesic activity and side-effects in 104 hospitalized postoperative patients. Butorphanol proved to be 30 to 40 times as potent as meperidine on a weight basis. Both medications provided maximum pain relief approximately 1 hr after administration. The most common side-effect in all groups was drowsiness. 9 references. (Author abstract modified)

001663 Giraldi, G.; Mandracchia, G. Ospedale Psichiatrico Provinciale, Gorizia, Italy **Clinical research on the collateral disinhibiting effects of a new kind of benzodiazepine drug clonazepam.** Indagine clinica sugli effetti collaterali disinibitori di una recente benzodiazepina (il clonazepam). Rassegna di Studi Psichiatrici (Siena). 65(5):989-996, 1976.

A new drug, clonazepam, of the benzodiazepine group, was administered to 12 patients: two epileptics, and one hebephrenic, one schizophrenic, a paranoid schizophrenic, five chronic schizophrenics, one phrenasthenic, a 17-year-old patient with violent impulses, and one patient with a depressive state. Results showed clonazepam produced a disinhibiting effect which, however, disappeared after a short time if dosage was not increased. Some patients reported fatigue, insomnia, ataxia, vertigo, and slight hypertension. 7 references.

001664 Gulmann, N. C.; Bahr, B.; Andersen, B.; Eliassen, H. M. M. Department for Men, Amtshospitalet i Vordingborg, DK-4760 Vordingborg, Denmark **A double-blind trial of baclofen against placebo in the treatment of schizophrenia.** Acta Psychiatrica Scandinavica (Kobenhavn). 54(4):287-293, 1976.

Twenty male chronic schizophrenic patients participated in a double-blind between patient study of the GABA like drug baclofen to evaluate the antipsychotic effect. No difference was found between the 10 patients who received baclofen and the 10 who received placebo with regard to the number of days before worsening of their psychiatric condition necessitated treatment with chlorpromazine, the total score for psychotic symptoms before and after treatment for 10 weeks, or the total consumption of chlorpromazine. Discontinuation of baclofen did not exacerbate the psychotic symptoms. Baclofen was superior to placebo in the treatment of anxiety, which is of particular interest in view of the recent theories of the mechanism of action of benzodiazepines. The relationship between the gabergic system and the dopaminergic system with regard to the substantia nigra and the corpus striatum is discussed as well as the suggestion, based on animal experiments, that Baclofen has an antipsychotic effect. 25 references. (Journal abstract modified)

001665 Haraszti, Joseph; Garver, David; Dekirmenjian, Harry; Pandey, G. N.; Chang, Sidney; Davis, John M. Illinois State Psychiatric Institute, Chicago, IL **Blood levels, drug interactions and dosage in psychiatric clinical pharmacology.** Journal of Psychiatric Research (Oxford). 13(1):58-59, 1976.

In a summary of a paper read before the Psychiatric Research Society, New York, October 31 to November 1, 1975, the design of studies concerning blood levels and drug

interactions and dosage whose solution may allow for increased application of clinical pharmacology to psychiatry is examined. Absorption of neuroleptic agents are illustrated by studies showing interactions between Gelusil and phenothiazines. Distribution and binding of neuroleptic agents are illustrated by studies showing variations in red blood cell binding among subjects with similar plasma levels and by correlating the appearance of dystonic reactions with red blood cell bound neuroleptic rather than plasma levels. Metabolism and excretion of the neuroleptic are illustrated by pharmacokinetic curves showing widely different half-lives of a phenothiazine and wide differences in steady state neuroleptic plasma levels between individuals. Such differences can be related to the appearance of hypotension in some neuroleptic treated subjects. Evidence relevant to defining dose response curves for antipsychotics are presented from a current study relating the effects of high, loading doses of neuroleptics vs standard dosage with respect to speed of response or ultimate clinical course. (Journal abstract modified)

001666 Harris, A. M.; Woollard, K. V.; Tweed, J. A. Cardiac Department, Charing Cross Hospital, London, England **A study of once daily tenormin (atenolol) in hypertension: some implications in patient compliance.** *Journal of International Medical Research* (Northampton). 4(5):347-351, 1976.

A clinical study is described in which hypertensive patients on no drug therapy were given atenolol in increasing doses from 50mg twice daily to 200mg twice daily until the diastolic blood pressure was 90mm Hg or below. At this stage the drug was withdrawn until blood pressure readings had risen to pretreatment levels. The same dose of atenolol was then reintroduced but now given once (in the morning) and was continued for 4 weeks. Of the 11 patients entering the study, 1 withdrew as his blood pressure was not controlled on a dose of 200mg of atenolol twice daily, and another because on withdrawal of atenolol his blood pressure did not rise to pretreatment levels. The remaining nine patients completed the study. There was a statistically significant fall in blood pressure on both atenolol regimes, and there was no significant difference between the blood pressure control achieved on twice a day and once a day administration. Only one patient developed side-effects; this being an asthmatic who developed mild dyspnoea on atenolol which did not necessitate withdrawal of the drug. It is concluded that once a day administration of a given dose of atenolol is therapeutically equivalent to twice a day administration. The implications of this in terms of better patient compliance, and thus better prognosis, are discussed. 27 references. (Author abstract)

001667 Hindmarch, Ian. Department of Psychology, University of Leeds, Leeds LS2 9JT, England **A sub-chronic study of the subjective quality of sleep and psychological measures of performance on the morning following night time medication with temazepam.** *Arzneimittel-Forschung* (Aulendorf). 26(11):2113-2116, 1976.

The hypnotic effects of temazepam were studied in 30 volunteers, 16 males and 14 females, with an average age of 28 years, recruited by advertising. Subjects with a history of psychiatric illness were excluded, as were subjects who had taken medication within the preceding 3 months. The subjects took placebo on the first night 1/2 hour before retiring, temazepam on the next 4 nights, and placebo on the last 6 nights. On each of the 11 test mornings, subjects were assessed on the sleep evaluation questionnaire, critical flicker fusion threshold, and choice reaction time. A clear dose response relationship was seen in the subjective and objective

measurements with the three doses used. A rebound phenomenon was seen only at the high dose levels and only in falling asleep and in behavior following awakening. 8 references.

001668 Karsten, Dieter J. Kuusankoski, Finland **Treatment of psychic disturbances of oligophrenics with new psycho-active long acting agent RP 19552 (piportyl palmitate).** *Acta Psychiatrica Scandinavica* (Kobenhavn). Supplement 265:21, 1976.

A summary of a report on the treatment of oligophrenics with a new long-acting psychoactive drug, given at a symposium on psychiatric prevention and crisis intervention held in June 1976 at Turku, Finland, is presented. RP 19552 (piportyl palmitate) was administered to a sample of 30 psychotic, severely agitated or aggressive, institutionalized oligophrenic patients once monthly for a period of 12 months. The preparation yielded good results in 11 cases, marked improvement in 4 cases, slight improvement in 4 cases, no improvement in 8 cases. Side-effects were generally mild, although in 12 cases they required Akineton treatment for less than a few days. In eight cases the therapy was discontinued after 4 weeks because of severe side-effects which in three cases lasted the whole period. The time saving due to the necessity of only one injection per month is considerable, but the preparation is unsuitable for outpatients use because of the often unpredictable extrapyramidal side-effects.

001669 Lasagna, Louis. Department of Pharmacology, University of Rochester School of Medicine, 601 Elmwood Avenue, Rochester, NY 14642 **Drug discovery and introduction: regulation and overregulation.** *Clinical Pharmacology and Therapeutics*. 20(5):507-511, 1976.

The effect of drug regulation on the discovery and use of drugs is considered in terms of drug innovation and improvement, potential curative functions, and excessive and prolonged negotiations with Federal regulatory agencies. Four cause and effect relationships between increased drug regulation and decreased new chemical entities (NCE) are examined: difficulty of process mandates less likelihood of success in introducing NCEs; amount of research possible for a given NCE research budget decreases with either general inflation or specific inflation occurring when the drug development process becomes disproportionately more expensive; a change in recent years in Federal Food and Drug Administration regulatory policy due to academic/professional/industrial complaints has coincided with a partial closing of the foreign/United States drug gap in NCEs available; and the notion that NCEs are limited by an exhaustion of biological knowledge is contradictory to the exponential rate of increase in basic knowledge about both disease and drugs. It is concluded that highly technical matters such as NCE research and development are poorly handled by representative and regulatory processes, such as those required in Federal management. 2 references.

001670 Lescovelli, M.; Castellani, A.; Perbellini, D. Ospedali Neuropsichiatrici Provinciali, Piazza Lambranzi 1, I-37034, Marzana-Verona, Italy **A double-blind cross-over evaluation of the activity of D-oxazepam hemisuccinate sodium salt (D-7-chloro 1,2-dihydro-3-hemisuccinyloxy 5-phenyl-2H-1, 4-benzodiazepine-2-one) compared to its racemic form.** *Arzneimittel-Forschung* (Aulendorf). 26(8):1623-1626, 1976.

D-Oxazepam hemisuccinate sodium salt was compared with its racemic form in 34 chronic psychiatric inpatients in whom anxiety was the main symptom. The 16 males and 18 females

ranged in age from 23 to 78 years, with a mean age of 53 years. Diagnoses were neurosis in 10, psychosis in 8, mental retardation in 7, involutional depression in 6, and addiction in 3. The study utilized a double-blind crossover design, with the patients receiving each drug for 9 days. Patients were rated on the Hamilton Anxiety Scale before treatment and every 3 days thereafter. D-oxazepam hemisuccinate was effective in insomnia, anxiety states, and somatic symptoms associated with anxiety, and was more active than the racemic form. Side effects were muscle weakness, dry mouth, and daytime sleeping. 8 references.

001671 Ludin, H. P.; Kunz, F.; Lorincz, P.; Ringwald, E. Neurolog. Universitäts-Klinik, Inselspital, CH-3010 Bern, Switzerland /Clinical experiences with bromocriptin, a central dopaminergic stimulator./ Klinische Erfahrungen mit Bromocriptin, einem zentralen dopaminergen Stimulator. Nervenarzt (Berlin). 47(11):651-655, 1976.

A clinical trial was made of bromocriptin (CB 154) in 52 patients with vascular or idiopathic parkinsonism. In open experiments the drug led to significant reduction in akinesia, rigor, and tremor. In double-blind comparison with levodopa, amantadin, and trihexyphenidyl (eight patients each) bromocriptin was effective in 62% of patients, amantadin and levodopa in 50%, and trihexyphenidyl in 12%. Bromocriptin was administered to 37 patients for more than 6 months, and to 12 patients for more than 1 1/2 years without losing its efficacy. Its tolerance was good in slowly increasing dosage, the most frequent side-effect being nausea. 10 references. (Author abstract modified)

001672 Marie-Cardine, M.; Merel, J. P. no address /Clinical trial of sultopride./ Essai clinique du sultopride. Semaine des Hôpitaux: Thérapeutique (Paris). 52(9):512, 1976.

A summary is given of a clinical trial of sultopride which was presented at the 73rd Congress of Psychiatrists and Neurologists of the French Language held at Nîmes in June and July, 1975. Sultopride was given to patients with manic states and agitation crises. Its action was found to be rapid. One extremely intense manic state was reduced in 48 hours with such efficacy that the patient was able to leave the hospital on the third day. Tolerance of the drug was excellent, with the exception of extrapyramidal effects, which rapidly appeared.

001673 Reale, Attilio; Nigri, Antonio; Gioffre, Pier Agostino. II Cattedra Malattie Cardiovascolari, University of Rome, Rome, Italy Evidence for improved cardiac performance after beta-blockade in patients with coronary artery disease. Journal of International Medical Research (Northampton). 4(5):338-346, 1976.

The acute hemodynamic effects of bunitrolol a cardioselective beta-blocker with partial agonist activity were investigated. Right and left heart catheterization was performed in 11 patients with documented coronary artery disease. After bunitrolol there was a statistically significant decrease in left ventricular and aortic systolic pressures, left ventricular end/diastolic pressure, aortic diastolic and mean pressures, pressure rate product, and compliance index. Left ventricular dp/dt, left ventricular dp/dt over isovolumic pressure, systemic resistance, and heart rate tended to decrease; stroke volume and left ventricular stroke work index tended to increase, without statistical significance. Cardiac index showed individual variations, the mean values for the group being unchanged. Correlation of left ventricular end/diastolic pressure and left ventricular stroke work index showed a shift toward improved ventricular function curve in most cases,

deterioration in no instance. Supine exercise was performed in 10 patients. Angina occurred in nine patients; in five only before, and in four before and after beta-blockade. It is concluded that certain beta-blockers can improve cardiac performance at rest and during exercise in patients with coronary artery disease. This is explainable on the basis of a more favorable balance between oxygen supply and demand, together with a less marked negative inotropic effect due to the partial agonist activity of bunitrolol. 25 references. (Author abstract)

001674 Rees, J. A.; Risdall, P. C. Boots Co. Ltd., Nottingham, England An evaluation of a once daily dosage regime of dothiepin hydrochloride (Prothiaden). Journal of International Medical Research (Northampton). 4(5):319-325, 1976.

Tolerance of a 75mg single dose of dothiepin was tested in 105 depressed patients with or without symptoms of anxiety. The severity of their condition was such that treatment by the general practitioner with a tricyclic antidepressant without referral to a psychiatrist was suitable. Results indicate that the single daily dose regimen was well tolerated and efficacious. Compared to a thrice daily regime, the once daily dose appeared to be more beneficial on symptomatic insomnia during the early treatment period. 4 references. (Author abstract modified)

001675 Rooke, K. C. Worthing, West Sussex, England The use of flurazepam (dalmene) as a substitute for barbiturates and methaqualone/diphenhydramine (mandrax) in general practice. Journal of International Medical Research (Northampton). 4(5):355-363, 1976.

Flurazepam was substituted for habitually used barbiturates or methaqualone/diphenhydramine in a practice with a higher than average geriatric population. The purpose of the study was to substitute flurazepam for habitually used barbiturates or methaqualone/diphenhydramine. Of the original 53 patients admitted to the study, 51 completed; the 2 dropouts resulting from concomitant physical illness. Eighty four percent of patients were successfully changed to flurazepam. Of those who did not accept flurazepam, 8% accepted nitrazepam, while 6% of patients were motivated to stop all hypnotics. During the 3 month period of the study none of the well known disadvantages of the barbiturates and methaqualone/diphenhydramine were seen with flurazepam. Flurazepam was found to be a very efficient hypnotic of relatively low toxicity which could be easily substituted for barbiturates and methaqualone/diphenhydramine diphenhydramine in the treatment of long-term insomnia. 10 references. (Author abstract)

001676 Sechzer, Philip H. Department of Anesthesiology, State Univ. of New York at Maimonides Medical Center, Brooklyn, NY Demand method evaluation of hypnotics. Current Therapeutic Research. 19(5):637-644, 1976.

Development of a demand method for evaluating hypnotic effects of a new benzodiazepine derivative, lorazepam, is reported. Lorazepam is a potent psychotropic possessing strong anticonvulsant, antimorphine, and antitremor properties in animals. Basic demand data were supplemented with a combined survey of 100 subjects' assessment of a good nights sleep and nurses' objective observations. Active control was provided by reference to pentobarbital. Satisfactory sleep was associated with 3.75 to 4.0mg. lorazepam. For comparable results with pentobarbital 150 to 200 mg. were required. 4 references. (Author abstract modified)

001677 Vartanian, V.; Lazzaretto, R. Ospedale Generale Provinciale di Cittadella, Divisione Neurologica, Cittadella, Italy / *Posological and clinical study of maprotiline, a new drug with antidepressant action.* / Studio posologico e clinico di un nuovo farmaco ad azione antidepressiva: la maprotilina. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(2):519-528, 1976.

Efficacy and the tolerability of maprotiline, a new antidepressant drug, is evaluated. Drug was tested on 32 female patients, 20 to 64 years old, who were suffering from depression and had been hospitalized. Drug was administered to 12 patients intravenously and to the other 20 per os. Of these 20 subjects, 10 were treated with maprotiline and the other 10 with amitriptyline, both groups being tested double-blind. Conclusion was that in both groups maprotiline showed a clear antidepressant action which began to be manifested on the 5th day when given intravenously and on the 12th day when per os. Good tolerability was evidenced in both trials. 17 references.

001678 Widerlov, E. Psychiatric Research Centre, Ulleraker Hospital, 750 17 Uppsala, Sweden A comparative double-blind study of the side effects of Litarex and Lithionit Durettes. Acta Psychiatrica Scandinavica (Kobenhavn). 54(4):294-302, 1976.

Side effects of two lithium salts of a sustained release preparation were compared in a double-blind crossover study of 18 patients with unipolar or bipolar manic-depressive disease. The drugs compared were lithium citrate (Litarex, Dumex, Ltd.) and lithium sulphate (Lithionit Durettes, Hassle, Ltd.). After the patients had been adjusted to a serum concentration of 0.8 to 1.2 mmol/l, self-assessment of the frequency and intensity of 16 side-effect variables was performed during a period of 4 weeks. The most common side-effects were tremor, fatigue, polyuria, polydipsia, and reduced power of concentration. There was no difference in the frequency or intensity of side-effects between the two drugs. The side effects, are, accordingly, considered an effect of the lithium ion, rather than of the lithium salt. The difference in the size and appearance of the tablets was of very little practical significance. 18 references. (Journal abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

001679 Bilikiewicz, Adam. Klinika Chorob Psychiczych, Akademia Medyczna, Gdansk, Poland / *Neuroleptic drugs with time release action for use in schizophrenic psychosis.* / Leki neuroleptyczne o przedluzonym działaniu w leczeniu psychoz schizofrenicznych. Psychofarmakoterapia Schizofrenii Lek o Przedluzonym Działaniu. Wrocław, Polskie Tow. Psychiat. Odd. Wrocławski, 1976. 256 p. (p. 17-33).

In a paper presented at a symposium on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wrocław, Poland, in October 1973, neuroleptic drugs with time release action for use in schizophrenic psychosis are examined as to dosage and efficacy. On the basis of an extensive literature search the study concludes that neuroleptic drugs are especially useful in a time release form for treatment of schizophrenia. Their use however requires many conditions, cautions and judicious individualized use of the drug. The drug selection, dosage and frequency, as well as the use of Parkinsonism inhibitors must be considered. Drugs discussed include fluphenazine depot, thioridazine retard, flupenthixol depot, and fluanxolem depot. 40 references.

001680 Brambilla, F.; Guastalla, A.; Guerrini, A.; Rovere, C.; Legnani, G.; Sarno, M.; Riggi, F. Clinica Psichiatrica

dell'Universita, Via Besta 1, Milano Affori, Italy *Prolactin secretion in chronic schizophrenia.* Acta Psychiatrica Scandinavica (Kobenhavn). 54(4):275-286, 1976.

Basal prolactin secretion and its response to various stimuli were studied in 20 chronic hebephrenic schizophrenics, 10 males and 10 females, aged 20 to 54. The duration of the disease varied between 4 and 30 years. Eight normal subjects from the hospital staff, four males and four females, matched for age, served as controls. The patients had been off medication for 10 days in 17 cases, for 3 months in one case, and for 1 year in two cases. Schizophrenics only were subjected to a 2 day therapy with chlorpromazine and thereafter for 8 days to a combined therapy with chlorpromazine at the same dose plus 2-Br-alpha-ergokryptine-mesilate. Prolactin levels were assayed radioimmunologically in the basal condition, during the TRH stimulation test, after 2 days of combined drug therapy. The results obtained showed normal basal prolactin levels, significantly enhanced responses to TRH, and normal increases after 2-Br-alpha-ergokryptine-mesilate. A possible relative catecholamine deficiency, related to the mental disease, is suggested to explain the results. 37 references. (Journal abstract modified)

001681 Brambilla, F.; Rovere, C.; Guastalla, A.; Guerrini, A.; Riggi, F. Endocrine Center, Ospedale Psichiatrico Provinciale, Paolo Pini, Via Ippocrate, 45, Minalo-Affori, Italy *Gonadotropin response to synthetic gonadotropin hormone-releasing hormone (GnRH) in chronic schizophrenia.* Acta Psychiatrica Scandinavica (Kobenhavn). 54(2):131-145, 1976.

Gonadotropin hormone releasing hormone (GnRH) stimulation tests were performed in 15 adult male hebephrenic schizophrenics and 15 oligophrenic controls, matched for age and length of hospitalization. GnRH was given at three dosage levels to five subjects of each type, and levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH) in the blood were assayed at intervals up to 90 minutes. The tests were performed twice in schizophrenics off therapy and after 10, 20, and 30 days of chlorpromazine therapy. Controls were not given chlorpromazine and were tested only twice. Schizophrenics showed relative increases in both FSH and LH that were greater than those of controls, and the response persisted longer. Chlorpromazine had no effect on the test. 30 references. (Author abstract modified)

001682 Chien, Ching-Piao; Labrie, Richard; Park, Choong-Guen; Cole, Jonathan O.; Werner, William M. Albany Medical College, Albany, NY 12208 *Generic and trade-name antipsychotic drugs: clinical equivalence.* American Journal of Psychiatry. 133(12):1377-1381, 1976.

The clinical inequivalence of generic versus tradename drugs for psychotropic drugs and the methodological, sociological, and economic aspects of the evaluation of clinical equivalence of generic versus tradename drugs, particularly in light of the recent expiration of patents on some psychotropic drugs, is discussed. Methodology is emphasized in this report of a double-blind study of the efficacy of chlorpromazine and Thorazine in the treatment of 54 acute schizophrenic patients. An analysis designed to infer the maximum possible advantages of Thorazine over generic chlorpromazine indicated that differences between the two were clinically insignificant. 15 references. (Author abstract modified)

001683 Chouinard, Guy; Annable, Lawrence. Allan Memorial Institute, 1025 Pine Avenue West, Montreal, Quebec H3A 1A1, Canada *Penfluridol in the treatment of newly admitted schizophrenic patients in a brief therapy unit.* American Journal of Psychiatry. 133(7):820-823, 1976.

Penfluridol, a long acting neuroleptic that can be administered orally once a week, was compared with chlorpromazine in the treatment of 33 newly admitted schizophrenic patients in a brief therapy unit. Patients receiving either drug improved enough to be discharged in 3 weeks. Penfluridol treated patients experienced less drowsiness than those treated with chlorpromazine, but the severity of extrapyramidal symptoms appeared to be greater with penfluridol. 9 references. (Author abstract)

001684 Cowen, Murray A. Rockland Research Institute, Rockland State Hospital, Orangeburg, NY 10962 An electrophysiological study on the effects of tryptophan and cortisol on schizophrenic and other mentally ill patient groups and on normal subjects. *Biological Psychiatry*. 11(4):389-401, 1976.

In light of previous findings that cortisol very rapidly induces increased tryptophan hydroxylase activity in brain and that cortisol metabolism is disrupted in schizophrenics, the effects of mild tryptophan loading on schizophrenic and control groups of nonschizophrenic and normal subjects were assessed. Direct current potentials measured on the scalp suprajacent to the midline prefrontal cortex were used to monitor the metabolic activity, via carbon dioxide production, of this portion of the cerebrum. Changes in the frontal potential 90 minutes after oral administration of L-tryptophan cortisol were examined in 12 normal males, 10 nonschizophrenic male psychiatric patients, 6 normal females, and 30 schizophrenic patients. All normal and nonschizophrenic subjects showed a significant decrease in their frontal voltages, most marked in the females, after tryptophan loading. A nonsignificant voltage increase was produced by subsequent administration of cortisol. Tryptophan loading had an opposite, voltage increasing effect on the 30 schizophrenic subjects tested. This abnormal response was greatest in the male and postmenopausal schizophrenic subjects. Besides this sex effect, the abnormality increased with age up to a point, and was decreased by antipsychotic medication and cortisol. An explanation in terms of an abnormality in the relative hydroxylation of indoles in schizophrenic subjects is proposed. 54 references. (Author abstract modified)

001685 Crow, T. J.; Deakin, J. F. W.; Johnstone, E. C.; Longden, A. Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England Dopamine and schizophrenia. *Lancet* (London). 2(7985):563-566, 1976.

The correlation between observed antipsychotic actions and extrapyramidal side-effects of neuroleptic drugs and their ability to block central dopaminergic transmission is discussed. It is contended that antipsychotic effects are more closely related to actions of these drugs on dopaminergic mechanisms in the mesolimbic dopamine system, while extrapyramidal reactions are linked with similar actions in the striatum. It is noted that although amphetamine psychosis closely resembles paranoid schizophrenia and may be related to excess dopamine release, clinical, biochemical, and endocrine findings suggest that dopaminergic overactivity is not a necessary concomitant of schizophrenia. It is suggested that the primary defect in schizophrenia does not lie in the dopamine neuron, and that the exact nature of this defect is unknown. Possible explanations advanced include that of supersensitivity of the mesolimbic dopamine receptors and that of a deficit in a system which is normally antagonistic to the mesolimbic dopamine system. 54 references. (Author abstract modified)

001686 Donlon, Patrick T. Department of Psychiatry, School of Medicine, University of California at Davis, Sacramento,

CA 95616 High dosage neuroleptic therapy: a review. *International Pharmacopsychiatry* (Basel). 11(4):235-245, 1976.

The questions of the safety and efficacy of high dose neuroleptic therapy in human subjects resisting standard dose therapy or requiring rapid symptom remission are reviewed. This regimen seems indicated in some patients when the added risk of dose related adverse effects are weighed against the potential merit of treatment. By providing symptom remission, neuroleptic agents of various types allow physicians in the community to treat schizophrenic patients in all phases of illness. However, little definitive research in acute ambulatory patients is available. The physician is cautioned against applying efficacy and safety studies with chronic inpatients because of methodologic shortcomings of such studies, primarily that this patient subgroup may not be representative due to biological and psychological changes resulting from long-term institutionalization. Drugs discussed are fluphenazine, chlorpromazine, thiothixene, haloperidol and trifluoperazine. 29 references. (Author abstract modified)

001687 Ebstein, R. P.; Biederman, J.; Rimon, R.; Zohar, J.; Belmaker, R. H. Jerusalem Mental Health Center, Ezrath Nashim, PO Box 140, Jerusalem, Israel Cyclic GMP in the CSF of patients with schizophrenia before and after neuroleptic treatment. *Psychopharmacology* (Berlin). 51(1):71-74, 1976.

The possibility that alterations in central cholinergic activity, detectable by measurement of guanosine monophosphate (cyclic GMP) levels in cerebrospinal fluid (CSF), may play a role in the development of schizophrenia was investigated in 27 schizophrenic patient. The mean level of CSF cyclic GMP was 23% lower in drug free patients than in controls, but this difference was not statistically significant. The mean level of CSF cyclic GMP rose 50% in schizophrenic patients after 2 months of treatment with phenothiazines. It is suggested that decreased activity of central cholinergic neurons may be associated with schizophrenia, and that neuroleptic treatment restores dopaminergic/cholinergic balance. 30 references. (Author abstract modified)

001688 Eckmann, F. Krankenhaus für Psychiatrie und Neurologie Schleswig-Stadtfeld, D-2380 Schleswig, Germany /Double-blind clinical study of caripramine/placebo./ Klinische Prüfung von Caripramin/Plazebo im Doppelblindversuch. *Arzneimittel Forschung* (Aulendorf). 26(12):2224-2226, 1976.

A double-blind crossover study with caripramine and placebo was conducted in 30 long-term hospitalized schizophrenic patients. Caripramine was found to have a positive effect on the behavior of long-term hospitalized schizophrenic patients, but there were no differences in the effects of the drug on the productive form of schizophrenia versus the nonproductive form of the condition. Side-effects or complications of psychic, autonomic, and/or motor disturbances were not found. The usual laboratory tests showed no deviation from normal. 11 references. (Journal abstract modified)

001689 Garver, David L.; Davis, John M.; Dekirmenjian, Hartoune; Jones, Frank D.; Casper, Regina; Haraszti, Joseph. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, IL 60612 Pharmacokinetics of red blood cell phenothiazine and clinical effects: acute dystonic reactions. *Archives of General Psychiatry*. 33(7):862-866, 1976.

The pharmacokinetics of the phenothiazine and butaperazine (neuroleptics) are studied in relationship to acute dystonic reactions. Blood samples from schizophrenic patients undergo-

ing psychopharmacological therapy are used in the study. Dystonias appeared on falling drug concentrations, more than one half-life after plasma and red blood cell (RBC) peak butaperazine concentrations. Red blood cell butaperazine kinetics differentiated better than did plasma butaperazine levels in those subjects in whom dystonias would develop from those in whom they did not. It was felt that RBC phenothiazine levels may more clearly reflect drug concentration at critical brain sites than do simple plasma drug levels. Furthermore, dystonic reactions may be the result of differential sensitivity of two or more receptor systems to receptor blockade by antischizophrenic agents. 11 references. (Author abstract modified)

001690 Gonçalves, N. Psychiatrische Klinik der Freien Universität, Nussbaumallee 36, D-1000 Berlin 19, Germany /Changes of behavior in a group of hospitalized chronic schizophrenics treated with EMD 16 139, a benzocholinolizin derivate./ Veränderung des Antriebs bei hospitalisierten chronisch Schizophrenen unter der Behandlung mit EMD 16 139, einem Benzocholinolizinderivat. International Pharmacopsychiatry (Basel). 11(2):65-73, 1976.

A group of hospitalized chronic schizophrenic patients was treated with EMD-16139 -- a benzocholinolizin derivate -- for 4 weeks in a placebo controlled trial. Changes of behavior were measured using a rating scale. The results suggest an increase of activity and initiative during treatment. Problems concerning some neuroleptic effects are discussed. 4 references. (Author abstract)

001691 Hogarty, Gerard E.; Ulrich, Richard F.; Mussare, Frank; Aristigueta, Narciso. 3811 O'Hara Street, Pittsburgh, PA 15261 Drug discontinuation among long term, successfully maintained schizophrenic outpatients. Diseases of the Nervous System. 37(9):494-500, 1976.

Forty three drug maintained and 6 placebo maintained schizophrenics who had successfully completed at least 2 years of treatment in a controlled study of drug and social therapy were chosen as candidates for a drug discontinuation study. The subjects had met the criteria of being low rate for relapse and had remained on study medication since hospital discharge. Two patients terminated for administrative reasons, and 27 of the 41 remaining withdrawn patients (65.8%) relapsed in the year following initiation of drug withdrawal. The nature and extent of clinical change among the relapsed and nonrelapsed patients are tabulated. On dimensions of primary psychotic thinking as well as secondary symptoms and social dysfunctioning, patients judged to have relapsed following drug discontinuation are significantly more ill on nearly all measures reported by family, psychiatrist, and social worker. It is suggested that further research is needed on minimal maintenance dosage requirements. It is among responsive patients that have remained relatively asymptomatic and have demonstrated an ability to survive because of maintenance treatment that the problems of continued treatment and dosage become critical. 18 references.

001692 Isermann, H.; Haupt, R. no address Pathological alterations of the EEG during treatment with clozapin in patients with schizophrenic symptomatology. Electroencephalography and Clinical Neurophysiology (Amsterdam). 41(6):665, 1976.

At a meeting of the German EEG Society in Munster in 1975, the finding that long-term therapy with clozapin produces marked alterations in EEG in schizophrenic patients significantly more frequently than do other neuroleptics was reported. Pathological alterations in the EEG are revealed in

approximately 50% of the patients receiving older neuroleptic drugs and in almost every patient receiving clozapin. It is suggested that psychotropic drugs make the functional disturbance in the brainstem region, related to the schizophrenic illness, more obvious.

001693 Jacobsson, L.; Von Knorring, L.; Mattsson, B.; Peris, C.; Rapp, W.; Edenius, B.; Kettner, B.; Magnusson, K. E.; Villemoes, P. Department of Psychiatry, University of Umea, S-901 85 Umea, Sweden Controlled trial of penfluridol and thiothixene in the maintenance treatment of chronic schizophrenic syndromes. Acta Psychiatrica Scandinavica (Kobenhavn). 54(2):113-124, 1976.

A controlled trial was conducted of penfluridol (a diphenylbutylpiperidine derivative chemically related to pimozide and fluspirilene) and thiothixene (a thioxanthene derivative with a piperazine side chain) as maintenance drugs in patients with chronic schizophrenic syndromes. Some improvement over previous neuroleptics was seen with both drugs, mainly in variables concerned with participation in social activities as assessed with the S-scale and by ward behavior. Drug dosages necessary were very low and produced few and easily manageable side effects. There was no significant difference between the two drugs, but penfluridol has the practical advantage of being the only long acting drug for oral administration so far available. 15 references. (Author abstract modified)

001694 Jaroszynski, Jan. Klinika Psychiatryczna, Instytut Psychoneurologicznej, Warsaw, Poland /Indications for pharmacotherapy of schizophrenia./ Wskazania w farmakoterapii schizofrenii. Psychofarmakoterapia Schizofrenii Leki o Przegluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat. Odd. Wroclawski, 1976. 256 p. (P. 3-15).

In a paper presented at a symposium on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, indications for pharmacotherapy in schizophrenia are discussed on the basis of Polish bibliographic sources and research conducted at the Warsaw Psychiatric Clinic. Research was directed toward determination of the proper drugs for the various types of schizophrenia, with emphasis on certain atypical symptoms which nevertheless are relatively universal. The selection of the proper neuroleptic is based on its particular effectiveness in regard to specific physical and emotional disturbances. 24 references.

001695 Jobe, P. C. Department of Pharmacology and Therapeutics, Louisiana State University Medical Center, School of Medicine, Shreveport, LA Pharmacotherapy of schizophrenia. Current Concepts in Psychiatry. 2(3):6-11, 1976.

The pharmacological basis of schizophrenia and pharmacotherapy of schizophrenia are discussed. Schizophrenia is seen as the possible result of abnormal dopaminergic and noradrenergic transmission in specific areas of the brain. The probable reason for the effectiveness of the antipsychotic drugs in the treatment of schizophrenia is due to their capacity to normalize catecholaminergic transmission in these critical areas. No substantive evidence exists for the choice of any one of the more popular neuroleptics in the management of schizophrenia except for their differing side-effects. Techniques for dealing with noncompliance with the physician's prescription and drug maintenance therapy are discussed. 20 references.

001696 Karoum, Farouk; van Kammen, Daniel P.; Bunney, William E., Jr.; Gillin, J. Christian; Jimerson, David C.; Post,

Robert M.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, IRD, Saint Elizabeths Hospital, Washington, DC **The effect of probenecid on the free and conjugated 3-methoxy-4-hydroxyphenylglycol (MHPG) in lumbar cerebrospinal fluid.** *Psychopharmacology Communications*. 2(2):141-148, 1976.

Free 3-methoxy-4-hydroxyphenylglycol (MHPG) and conjugated MHPG in lumbar cerebrospinal fluid were measured before and after probenecid treatment in schizophrenic patients by a gas liquid chromatography/mass fragmentographic procedure. Neither the free MHPG nor the conjugated MHPG was appreciably altered by probenecid. Total MHPG was statistically increased by probenecid but not enough for the probenecid test to be clinically useful for estimating norepinephrine turnover from probenecid induced changes in MHPG concentrations. A modified mass fragmentographic method which permits direct measurement of free MHPG and conjugated MHPG is described. 30 references. (Author abstract modified)

001697 Kellner, Robert; Rada, Richard T.; Egelman, Arthur; Macaluso, Benedetto. Department of Psychiatry, School of Medicine, University of New Mexico, Albuquerque, NM 87131 **Long-term study of molindone hydrochloride in chronic schizophrenics.** *Current Therapeutic Research*. 20(5):686-694, 1976.

Twenty three chronic schizophrenic inpatients participated in an open label study of molindone hydrochloride and six patients were in an open label control group. The duration of the study ranged from 6 months to 19 months, with a median of 13.1 months. The side-effects, results of physical examinations, electrocardiograms and changes on laboratory investigations did not differ substantially from those of other antipsychotic drugs except that there was a tendency for patients to lose weight. The drug appeared to be less sedating than other antipsychotic drugs. The response to molindone was, on the whole, similar to the patients' previous and subsequent antipsychotic medications; however, a few patients appeared to be less well controlled, and two patients improved decidedly more than while taking their previous drugs. In view of the weight loss, molindone appears to be suitable for psychotic patients who are overweight. 8 references. (Author abstract)

001698 Kiloh, L. G.; Williams, S. E.; Grant, D. A.; Whetton, P. S. School of Psychiatry, Prince Henry Hospital, Little Bay, New South Wales 2036, Australia **A double-blind comparative trial of loxapine and trifluoperazine in acute and chronic schizophrenic patients.** *Journal of International Medical Research* (Northampton). 4(6):441-448, 1976.

A double-blind comparative trial of loxapine and trifluoperazine was carried out in 57 acute and chronic schizophrenic patients. In both groups of patients loxapine proved to be equivalent in its effects to trifluoperazine. There were suggestions it might be more effective in chronic patients. Side-effects were similar with the two drugs but anticholinergic effects, excitement, dizziness and faintness occurred more often with loxapine. Laboratory tests, urine analysis, cardiovascular and ophthalmological investigations showed no significant abnormalities. 16 references. (Author abstract)

001699 Kobayashi, Tsukasa. Sophia University, Tokyo, Japan **Medical and social influence of pharmacotherapy against schizophrenia.** *Psychiatria et Neurologia Japonica* (Tokyo). 78(1):73-81, 1976.

Under the premise that schizophrenia is not a disease, but a syndrome defined by certain persons showing certain symptoms, the medical and social impact of pharmacotherapy for schizophrenia since its introduction in the early 1950s is discussed. Medical tests of the major psychotropic drugs for schizophrenia are cited to conclude that patients receiving drug therapy are only relieved of their outward symptoms and not the roots of the syndrome. Changes that drug therapy has wrought on the families of the schizophrenics and the psychiatric profession are also discussed. The former have more hope that their schizophrenic member can be rehabilitated into society, while the latter has sometimes become content to treat the outward manifestations with drugs and abandon the patient. Pharmacotherapy is seen as an incomplete treatment and more psychoanalysis, home services, aftercare, long-term prescription of medication, efforts toward gradual withdrawal from medication, and attention to factors which cause psychological reaction in the patient are proposed. 35 references.

001700 Kuhn, R. Psychiatrische Klinik, CH-8596 Munsterlingen, Switzerland **Neuroleptic effect of baclofen in chronic schizophrenics.** / *Über die neuroleptische Wirkung von Baclofen bei chronisch Schizophrenen.* *Arzneimittel-Forschung* (Aulendorf). 26(6):1187, 1976.

To test its neuroleptic effect, baclofen (Lioresal) was given to 24 severe chronic schizophrenics in doses up to 75mg/day. Of these patients, 4 improved, 12 were unchanged, and 4 deteriorated. Patients who responded well had had acute symptoms or a history of depression, while some of those who deteriorated had catatonic symptoms. This new class of drugs merits further evaluation of psychopharmacological activity.

001701 Levenson, Alvin J.; Burnett, Gordon B.; Nottingham, John D.; Sermas, Chris E.; Thornby, John I. Department of Psychiatry, Baylor College of Medicine, Houston, TX **Speed and rate of remission in acute schizophrenia: a comparison of intramuscularly administered fluphenazine HCl with thiothixene and haloperidol.** *Current Therapeutic Research*. 20(5):695-700, 1976.

A double-blind controlled study compared three neuroleptic drugs (fluphenazine HCl, thiothixene and haloperidol), intramuscularly administered in predetermined and equipotent dosages, for rate and speed of remission in acute schizophrenics. The results of the study demonstrated this clinical approach to be extremely efficacious, producing a median time to remission of 9 days and an average remission rate of 83%. The lack of statistically significant intergroup difference suggests that the efficacy of these regimens is more related to the route of administration than the innate properties of the parenteral drug form. 18 references. (Author abstract)

001702 Levy, Deborah L.; Weinreb, Herman J. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Wheat gluten -- schizophrenia findings.** *Science*. 194(4263):448, 1976.

Some methodological criticisms of Singh and Kay's research (1976) on wheat gluten challenge in schizophrenics are presented. These are: 1) of 14 reported measures only 5 reached significance; 2) deterioration during gluten treatment occurred only in the five most seriously ill patients with less favorable therapeutic outcomes; 3) graph data did not indicate pathologic increases but decreasing trends during gluten treatment; 4) analysis of data would have required subgrouping of subjects by premorbid history and paranoid/nonparanoid

status; and 5) borderline IQ of the sample is not representative of hospitalized schizophrenics. It is concluded that appropriate statistical tests of the data and replication of the results are necessary to demonstrate that gluten does impair the psychological status of schizophrenics. 1 reference.

001703 Liebowitz, Jerome H.; Rudy, Victor; Gershon, Elliot S.; Gillis, Aaron. Albert Einstein College of Medicine, Bronx, NY A pharmacogenetic case report: lithium-responsive postpsychotic antisocial behavior. *Comprehensive Psychiatry*. 17(5):655-660, 1976.

A double-blind crossover study was performed in which lithium carbonate was administered to a 22-year-old man with a 6 year course of schizophrenic like psychotic episodes and personality deterioration manifested by antisocial behavior to determine whether an association exists between family history of affective disorder and lithium responsiveness. Lithium was found to be effective in reducing overt antisocial behavior as well as poor judgment, hyperactivity, impulsivity, and destructiveness. The use of family history is discussed as a heuristic device for revealing a spectrum of lithium responsive disorders. 21 references.

001704 May, Philip R. A. University of California at Los Angeles, 760 Westwood Plaza, Los Angeles, CA 90024 Rational treatment for an irrational disorder: what does the schizophrenic patient need? *American Journal of Psychiatry*. 133(9):1008-1012, 1976.

A review of the results of controlled studies of various chemotherapeutic approaches to schizophrenia to indicate the impact of antipsychotic drugs is provided. It is felt that although research evidence strongly supports the efficacy of pharmacotherapy, not all schizophrenic patients should receive antipsychotic drugs and/or other forms of treatment. Caution against doctrinaire attitudes is advised and advocacy of adjustment of goals and methods to meet various patient and situational needs is offered. 17 references. (Journal abstract)

001705 Moinet, Alain; Van Nuffel, Dirk. Avenue de Jette 108, B-1080 Bruxelles, Belgium High doses of Haloperidol in the treatment of 5 young schizophrenics in a therapeutic community *Acta Psychiatrica Belgica* (Bruxelles). 76(1):149-156, 1976.

The use of very high doses (30 to 70 mg) of Haloperidol within a therapeutic treatment program consisting of individual psychotherapy, family therapy and involvement in the therapeutic community is examined in the cases of five schizophrenic adolescents whose agitation created a threat to themselves and the therapeutic community. The institute had tried a variety of psychotherapeutic and chemotherapeutic approaches to no avail and high doses of Haloperidol were used as a last resort. The response to the high doses was a marked diminution of psychotic symptoms, such as hallucination, autism, agitation, lack of impulse control, enabling the patients to make use of the treatment program. In three cases, as the patient got involved in therapy, the dose of Haloperidol could be progressively reduced and even discontinued in one case.

001706 Nakagawa, Fusako; Koshino, Yoshifumi; Enokido, Hideaki. Department of Neuropsychiatry, Kanazawa University School of Medicine, Kanazawa, Japan Electroencephalograms in schizophrenia treated with psychotropic drugs. *Clinical Electroencephalography* (Osaka). 18(2):94-102, 1976.

Evidence is presented on research into the effects of such psychotropic drugs as chlorpromazine (CPZ) and pentothal on abnormal brainwave readings in schizophrenic patients. Dif-

ferent studies are cited on the appearance of monorhythmic theta burst, delta-waves and delta bursts, the union of spiked waves, and positive spike waves which are often noted in schizophrenic patients. Correlations are made with such phenomenon as the appearance of monorhythmic theta burst after 2 months of pharmacotherapy and improvement of schizophrenic symptoms. Other reports of correlations between clinical improvement through pharmacotherapy and changes in the above four types of brainwaves are cited. More of these clinical electroencephalographic correlations are promised in a future report. 24 references.

001707 Nielsen, N. P.; Reitano, S. Ospedale Psichiatrico Provinciale, Como, Italy /Therapeutic evaluation of pipotiazine palmitate in a group of schizophrenics./ *Valutazione terapeutica del palmitato di pipotiazina in un gruppo di schizofrenici*. *Rassegna di Studi Psichiatrici* (Siena). 65(5):957-988, 1976.

The effect of pipotiazine palmitate on a group of 12 schizophrenics is described. All patients were male and had already been treated with electroshock and pharmacotherapy without positive results in the Psychiatric Hospital at Como, Italy. Simplex, hebephrenic, and paranoid schizophrenics were represented in the group of patients, and they were treated for 6 months. Every month they were administered tests, including the BPRSE of Overall and Gorham, Sterkman's Rating Scale, Martens and Ponsson's S-Scale, Simpson and Angus' Rating Scale, Malm and Perris' Rating Scale for Collateral Effects, and EEG. Results confirmed that a general amelioration was evident in these patients and that after 10 months nine of the twelve patients continued to be treated and received doses of the drug every 4 weeks. Best results were seen in the simplex and hebephrenic schizophrenics. On the basis of these results it was positively concluded that pipotiazine palmitate has a prolonged antipsychotic action on the patient and can permit him to return to society quickly. The drug also has fewer collateral effects, precludes the revolving door phenomenon, and facilitates further therapeutic assistance. 62 references.

001708 Ogura, Chikara; Kishimoto, Akira; Nakao, Takehisa. Department of Neuropsychiatry, Tottori University, School of Medicine, Yonago City, Japan Clinical effect of L-dopa on schizophrenia. *Current Therapeutic Research*. 20(3):308-318, 1976.

The effectiveness of L-dopa as supplementary therapy for schizophrenia in patients who were not sufficiently improved by major tranquilizers or other agents alone was studied. The combined therapy was judged to be significantly effective, effective, or slightly effective in approximately 22% of the patients studied. Side-effects such as uneasiness, anorexia, and vomiting occurred in 17% of the patients. It is suggested that the use of amine precursors including L-dopa in schizophrenia deserves further examination. The potential usefulness of this type of therapy is discussed in the light of theories of the biochemical disturbances occurring in schizophrenic patients. 14 references.

001709 Okuma, Teruo; Koga, Itsuyuki; Uchida, Yasunori. Department of Psychiatry, Tottori University School of Medicine, Yonago, Japan Sensitivity to chlorpromazine effects on brain function of schizophrenics and normals. *Psychopharmacology* (Berlin). 51(1):101-105, 1976.

The effects of a single oral dose of chlorpromazine (CPZ) on percent time waking calculated from electroencephalographic recordings (% W-EEG) and on the electrodermal response (EDR) measured as number of EDR per minute in

schizophrenic patients and normal controls were investigated. Both %WtEEG and number of EDR were significantly decreased 3 hr after CPZ administration in normal subjects, but not in schizophrenic patients. The neural mechanism underlying the lower sensitivity to CPZ effects on brain function in schizophrenia is discussed. 15 references.

001710 Pascal, Jean-Charles; Lauzel, Jean-Pierre Service de Fitz-James VIII, Hôpital Psychiatrique, Clermont-de-l'Oise, F-60600 France /Study of the use of Moditen Retard (fluphenazine enanthate) and of Modecate (fluphenazine decanoate) in 20 chronic cases./ Etude de l'utilisation du Moditen Retard (oénanthate de fluphenazine) et du Modecate (decanoate de fluphenazine) a propos de 20 observations de malades très chroniques. Psychologie Médicale (Paris). 8(6):927-936, 1976.

Fluphenazine enanthate and fluphenazine decanoate were studied in 20 psychiatric patients hospitalized on a chronic ward. The 18 males and 2 females ranged in age from 25 to 69 years old, and 17 had been ill more than 10 years. Of the 20 patients, 11 were schizophrenic, 6 had nonschizophrenic psychotic states, and 3 had organic or psychogenic mental retardation. Half the patients received another major tranquilizer along with fluphenazine, and 18 patients received antiparkinsonian medication. Results were very good in 5 patients, good in 9, and null in 6. Three case reports are given. At the end of the study, all patients were placed on fluphenazine decanoate. 6 references.

001711 Petruch, F.; Schuppel, R.; Breyer, U. Neurologische Klinik, Universität Tübingen, Liebermeisterstrasse 18-20, D-7400 Tübingen, Germany /Change in drug catabolism in the liver under treatment with perazine./ Änderung des Arzneimittelabbaus in der Leber unter der Behandlung mit Perazin. Arzneimittel-Forschung (Aulendorf). 26(6):1154-1155, 1976.

The effect of perazine on the metabolism and excretion of phenazone was studied. Schizophrenics who had been treated over a long period of time with up to 1000mg/day perazine were studied. Plasma levels for perazine and desmethylperazine were determined in eight patients. The half-life of phenazone was 11.2hr in controls and 27.0hr in perazine treated patients. The clearance of phenazone averaged 18.9ml/min in the patients and 47.0ml/min in the controls. The ratio of 4-hydroxyphenazone to unchanged phenazone was 185/29 in the controls and 66/40 in the perazine treated patients. Thus, perazine appears to inhibit drug hydroxylation in the liver. 11 references.

001712 Petursson, H. Kleppspítalinn, Mental Hospital, Reykjavík, Iceland /Lithium treatment of a patient with periodic catatonia. Acta Psychiatrica Scandinavica (København). 54(4):248-253, 1976.

A case report of successful lithium treatment in a patient with long standing periodic catatonia is described. Various medical treatments had been tried with meager results. Since 1955 a number of phenothiazines had been tried, also with little improvement. Commencement of lithium treatment in 1964 caused a dramatic improvement in the patient's condition. For 9 years the patient remained totally asymptomatic. Lithium treatment was terminated in 1975 because of lithium intoxication with a diabetes insipidus like syndrome. The patient then became psychotic again and has since experienced periodic phases similar to the previous illness. The diagnostic validity of the case is discussed, and some possible explanations of the favorable response to lithium are mentioned briefly. 13 references. (Journal abstract modified)

001713 Polonowita, A.; James, N. MCl. Psychiatric Department, Cherry Farms Group of Hospitals, Dunedin, New Zealand /Fluphenazine decanoate maintenance in schizophrenia: a retrospective study. New Zealand Medical Journal (Dunedin). 83(563):316-318, 1976.

The efficacy of intramuscular fluphenazine decanoate was assessed by the comparison of the time spent in hospital predrug and postdrug treatment by 43 schizophrenia patients. Before fluphenazine decanoate was begun, there was little difference between the treated and the dropout (oral medication) group in the number of admissions, but those who dropped out had spent less time in psychiatric wards prefluphenazine. After the intramuscular drug regime started, the differences became very marked, the number of admissions being significantly greater and longer for those on oral medication. There was a highly significant decrease in the number of admissions and far fewer days were spent in hospital compared with the predrug period for those who remained on fluphenazine decanoate. Those on oral medication had no change in the number of admissions and actually spent more days in the hospital, and their condition deteriorated. 8 references.

001714 Reiser, David E.; Willett, Allan Brock. Outpatient Psychiatry Clinic, University of Colorado Medical Center, 4200 E. 9th Ave., Denver, CO 80220 /A favorable response to lithium carbonate in a "schizo-affective" father and son. American Journal of Psychiatry. 133(7):824-827, 1976.

It has recently been suggested that patients with mania are often misdiagnosed as having schizophrenia. A favorable clinical response to lithium carbonate is reported in a father and son with an apparent schizoaffective disorder. It is concluded that some patients with schizoaffective syndromes may respond favorably to lithium but caution that a favorable response in such cases does not absolutely confirm a diagnosis of mania. 15 references. (Author abstract)

001715 Simpson, George M.; Varga, Ervin; Haher, E. Janet. Rockland Research Institute, Orangeburg, NY 10962 /Psychotic exacerbations produced by neuroleptics. Diseases of the Nervous System. 37(7):367-369, 1976.

The adverse reactions of 13 schizophrenic patients to neuroleptics is described. In three cases there was a marked increase in psychopathology, which was treated by decreasing or discontinuing the neuroleptics. There was no response to anticholinergic drugs nor to an increase in dosage; rather, this treatment seemed to exacerbate the situation. Ten of the patients showed catatonic excitement or inhibition and several developed hallucinatory episodes; all of these exacerbations were terminated by anticholinergic injections. 20 references. (Author abstract modified)

001716 Singh, Man Mohan. Clinical Psychopharmacology Unit, Bronx Psychiatric Center, Albert Einstein College of Medicine, Bronx, NY 10461 /Diazepam in the treatment of tardive dyskinesia: preliminary observations. International Pharmacopsychiatry (Basel). 11(4):232-234, 1976.

The effect of diazepam on tardive dyskinesia developed in human schizophrenics while undergoing neuroleptic treatment was studied. Diazepam was found effective in controlling tardive dyskinesia which developed in three schizophrenic patients undergoing neuroleptic treatment, mostly with haloperidol. Existential problems and emotional upset seemed contributory to the dyskinesia. Therapeutic effect did not appear related to sedation. The results suggest that tardive dyskinesia is probably not due to the anticholinergic effects of

some neuroleptics, and that limbic mechanisms may be involved since diazepam acts mostly on limbic structures. 4 references. (Author abstract modified)

001717 Singh, Man Mohan; Kay, Stanley R. Clinical Psychopharmacology Unit, Bronx Psychiatric Center, Bronx, NY 10461 **Wheat gluten -- schizophrenia findings**. *Science*. 194(4263):449-450, 1976.

A reply to some methodological criticism by Levy, Weinreb and Smith (1976) on a study of the effects of wheat gluten on schizophrenia by Singh and Kay (1976) is presented. Since the therapeutic efficacy of neuroleptics is accepted, a therapeutic arrest or reversal during wheat gluten intervention followed by therapeutic enhancement after the intervention would be considered adequate evidence of the countertherapeutic effects of the gluten intervention. The statistical analysis used in the study took into account the heterogeneity of the schizophrenia and the medication. A longitudinal rather than a cross-sectional approach was used in order to better focus on the effects of the intervention. Of the 14 patients in the study, 10 were found to be adversely affected by wheat gluten. The purpose of focusing on the five poor outcome patients was to suggest that wheat gluten did not act by interfering with the activities of the drugs and that any pathogenic effects of gluten can only be manifest to the extent that the countereffects of the neuroleptics are unsuccessful. Finally, the mean IQ of the sample is felt to fall within the norm for schizophrenics. It is felt that the research decisions in the study represented the best compromise between conflicting considerations and that these decisions are sound. Further research is needed to determine the validity of findings for a pathogenic effect of wheat gluten. 2 references.

001718 Smith, James M. Office of Clinical Research, Harlem Valley Psychiatric Center, Wingdale, NY 12594 **Wheat gluten - schizophrenia findings**. *Science*. 194(4263):448, 1976.

Some methodological criticisms of Singh and Kay's research (1976) on the effects of wheat gluten challenge on schizophrenics are presented. These are: 1) chi-square analysis of correlated psychopathology dimensions are not valid; 2) the correlated T-test is also invalid because the rows are not independent; 3) since no control groups were studied, it is impossible to determine how much attenuation of clinical effect is due to gluten intervention and how much is due to the normal processes of recovery from a schizophrenic episode; and 4) it is unclear whether the clinical interviews were conducted by the nonblind principal investigator. In view of these considerations it is concluded that the hypothesis that wheat gluten is pathogenic in schizophrenia was not adequately confirmed. 2 references.

001719 Van Den Berg, C. J. Department of Psychiatry, University of Groningen, Oostersingel 59, Groningen, The Netherlands **Gabergic compounds and schizophrenia**. *Lancet* (London). No. 7998:1301-1302, 1976.

In a letter to the editor, exception is taken to the suggestion that sodium valproate be used in treatment of schizophrenia which was based on the presumed involvement of gamma-aminobutyric acid (GABA) in schizophrenia and on the presumed action of sodium valproate on GABA. It is argued that in the current state of knowledge it seems impossible to decide whether an increase in GABA is directly related to the anticonvulsive or other properties of this compound. It is suggested that there might be other mechanisms by which sodium valproate could exert its actions. It is concluded that the literature on GABA in the past 25 years and on schizophrenia over

many more years is too complex for simple theories such as GABA deficiency in schizophrenia.

001720 Varkonyi, Bendeguz; Perenyi, Gabriela. Outpatient Clinic of the Hungarian State Railroads, Neurological Special Clinic, Budapest, Hungary **The role of Opar in the resocialization of schizophrenics**. *Rolle von Opar in der Resozialisierung schizophrener Kranken*. *Psychopharmakotherapie Schizophrenie*. Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat. Odd. Wroclawski, 1976. 256 p. (p. 89-93).

In a paper presented at a symposium on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a study of the role of Opar tablets, a fluorobutylpiperidine derivative, in the resocialization of schizophrenics is presented. Clinical test results indicate that the compound is long lasting, is not hypnosedative, is not hypotensive and lacks other autonomous reactions. Toxic rates are more favorable than with haloperidol. Of 36 male and 38 female patients, 26 to 72 years old, only 5 relapses occurred in the course of the study and further investigations showed that the patients had not continue their doses of Opar tablets. The drug is best indicated for patients who are in the process of resocialization but who still need outside assistance.

001721 Watts, Geoff. *New Medical Journals*, Clareville House, 26-27 Oxendon Street, London SW1Y 4EL, England **Drug research on treatment of schizophrenia**. In search of better connections. *World Medicine* (London). 11(21):27-28, 31, 1976.

Current research on a drug for the treatment of schizophrenia is reported, and the lack of orchestration in the disease is discussed. Thirty schizophrenics are undergoing test trials using piracetam (2-pyrrolidone acetamide) to determine whether or not the drug has an effect on information transference from one brain hemisphere to the other. Each schizophrenic will receive drug/placebo for 1 month followed by a 2 week washout and a further month of drug/placebo. During that time the patients will be clinically assessed by interview and on the wards and will undergo a series of tests on the factors over which piracetam might be expected to have some influence -- visual, auditory, and tactile stimuli. The patients will also undergo tests for memory and vigilance. According to Stuart Dimond, who is conducting the tests at University College, Cardiff, prior tests with students have demonstrated that administration of piracetam enhances verbal and auditory memory. While the mechanism by which piracetam brings about such effects is unclear, one suggestion is that the drug increases the amount of effective gamma-aminobutyric acid in the brain, bringing it into a more effective state of action.

001722 Westerink, Ben H. C.; Korf, Jakob. Laboratory for Pharmaceutical and Analytical Chemistry, Dept. of Clinical Chemistry, State University, Groningen, The Netherlands **Dopamine and schizophrenia**. *Lancet* (London). No. 7997:1249-1250, 1976.

The significance of the research of Dr. Crow which relates increases of homovanillic acid levels in the nucleus accumbens, observed after treating rats with various neuroleptics, directly to the dopamine receptor blocking activities of this compound is questioned. Research showing drugs which raise homovanillic acid levels yet lack dopamine receptor blocking activities is considered, and it is noted that many nonneuroleptic drugs can influence dopamine metabolism in such a way that high doses of such drugs as thioridazine and clozapine can interfere. The usefulness of the dopamine hypothesis in

developing new drugs is considered limited, and it is suggested that attention should extend from the dopamine neuron to the nondopaminergic neurons in the brain through investigation of the actions of such drugs as propranolol and sulpiride as antischizophrenic drugs.

001723 Woggon, B.; Angst, J. Psychiatrische Universitätsklinik, Forschungsdirektion, Lengstr. 31, CH-8029 Zurich 8, Switzerland / **Activity profile of caripramine: results of an open trial and a double-blind trial versus doxepin.** / Das Wirkungsprofil von Caripramin: Ergebnisse einer offenen Prüfung und einer Doppelblindprüfung gegen Doxepin. *Arzneimittel-Forschung (Aulendorf)*. 26(12):2226-2230, 1976.

An uncontrolled trial was conducted in which caripramine was administered to 39 patients with endogenous depression, five patients with schizoaffective psychoses, and two patients with paranoid schizophrenia with depressive syndromes in order to assess its effects on these patients. A clear antidepressant effect of the drug was demonstrated by clinical impression of improvement and by the results of the Hamilton rating scale for depression. A double-blind trial in which 14 patients were treated with caripramine and 16 patients were treated with doxepin was also conducted. Most patients suffered from endogenous depression with paranoid symptoms or from schizophrenia with depressive syndromes. Caripramine demonstrated both antidepressant and antipsychotic effects. No significant differences between caripramine and doxepin were noted. Caripramine was very well tolerated. It is concluded that caripramine can be classified as a nonsedative antidepressant with an antipsychotic effect. 5 references. (Journal abstract modified)

001724 Yu, Michio. Department of Neuropsychiatry, Tokyo Medical and Dental University, Tokyo, Japan **Thoughts on pharmacotherapy for schizophrenia.** *Psychiatria et Neurologia Japonica* (Tokyo). 78(4):350-354, 1976.

The theory behind and the action of various types of psychotropic drugs on schizophrenia is discussed. These neuroleptics are not confined to the treatment of schizophrenia and in addition to having tranquilizing and antianxiety effects, many have other characteristics which are taken into account during prescription and dosage fixage. Many have side-effects on the pyramidal fascicle - which many consider essential to the treatment of schizophrenia. This is an especially common opinion since the introduction of phenothiazine. The action of dopamine on brain nerve cells is explained through diagrams. Here, the dopamine acts to increase the functions of the dopaminergic neuron. This function of dopamine is the basis for understanding all neuroleptic effects. 4 references.

001725 Zavodnick, Steven. Dept. of Psychiatry and Human Behavior, Thomas Jefferson University Hospital, 11th and Walnut Streets, Philadelphia, PA 19107 **Suggestions for a rational approach to the chemotherapy of schizophrenia.** *Diseases of the Nervous System*. 37(12):671-675, 1976.

Suggestions for a rational approach to the chemotherapy of schizophrenia are offered because, it is claimed, current psychiatric practice does not seem to have kept pace with clinical psychopharmacology. Polypharmacy, inadequate dosage, overly brief drug trials, and erratic medication changes are commonplace. Psychopharmacology is obligated to disseminate the most current thinking in usable form and psychiatry has the responsibility of attempting to implement it in clinical practice. Based on pharmacologic, theoretical, and technical reasons, it is suggested that the use of high potency neuroleptics for the routine treatment of schizophrenia be

adopted and that low potency drugs be relegated to secondary status. Routine employment of higher standard neuroleptic doses is advanced to minimize the effects of individual variations in compliance, absorption, and metabolism. Also, a suggested protocol for the acute treatment of schizophreniform disorders is offered. 38 references. (Journal abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

001726 Anderson, William H.; Kuehne, John C.; Catanzano, Donna M. Harvard Medical School, Boston, MA **Rapid treatment of acute psychosis.** *American Journal of Psychiatry*. 133(9):1076-1078, 1976.

The effectiveness of haloperidol in the treatment of acute functional psychoses was investigated in 24 patients. Intramuscular injections of haloperidol produced almost complete remission of cardinal symptoms (thought disorder, hallucinations, and delusional activity) in 11 patients within 3 hours. Acute dystonia, easily reversed, was the only significant side-effect. It is suggested that outpatient management may be feasible and preferable in the treatment of some acute psychotic episodes. 13 references. (Journal abstract modified)

001727 Avery, David; Winokur, George. Palo Alto Veterans Administration Hospital, Palo Alto, CA **Mortality in depressed patients treated with electroconvulsive therapy and antidepressants.** *Archives of General Psychiatry*. 33(9):1029-1037, 1976.

The treatments of 519 depressed patients hospitalized from 1959 to 1969 were compared in a three year followup study with particular reference to mortality. The electroconvulsive therapy (ECT) group had a significantly lower mortality than the inadequate antidepressant treatment group and the group that received neither ECT nor antidepressants. Although the adequate antidepressant treatment group had a low mortality, statistically significant differences between this and other treatment groups could not be documented. Nonsuicidal deaths and particularly myocardial infarctions were significantly more frequent in the inadequately treated group compared to the adequately treated group. The results indicate the importance of adequate treatment of depression, especially in the older man. 49 references. (Author abstract modified)

001728 Beckmann, H.; Heinemann, H. Psychiatrische Klinik und Poliklinik, Universität München, Nussbaumstrasse 7, D-8000 Munich 2, Germany / **d-Amphetamine in the manic syndrome.** / D-Amphetamine beim manischen Syndrom. *Arzneimittel-Forschung (Aulendorf)*. 26(6):1185-1186, 1976.

The effect of amphetamine on manic behavior was studied in six patients, four men and two women, 20 to 55 years old, average age 28.6 years. Patients were rated on the Biegel Checklist for Mania by two psychiatrists. Two patients received 30mg d-amphetamine in an i.v. infusion over a period of 30 min; the other four patients received 50mg d-amphetamine by the same method. Patients were rated 0, 1/2, 1 1/2, 2 1/2, 3 1/2, and 4 1/2 hr following beginning of the infusion. All patients showed sedation and a decrease in mania lasting 3 hr. The decrease in mania was significant only in those patients who were elated euphoric, not in the patients who were paranoid destructive. There was no complete recovery from mania. 16 references.

001729 Beckmann, Helmut; Van Kammen, Daniel P.; Goodwin, Frederick K.; Murphy, Dennis L. Nervenkrankheiten der Universität München 2, Nussbaumstrasse 7, Munich, Germany **Urinary excretion of 3-methoxy-4-hydroxyphenylglycol in depressed patients: modifications by amphetamine and lithium.** *Biological Psychiatry*. 11(4):377-387, 1976.

The excretion of 3-methoxy-4-hydroxyphenylglycol (MHPG), the urinary metabolite which may best reflect brain norepinephrine, was measured in eight depressed patients on a longitudinal basis during the administration of placebo, d-amphetamine and l-amphetamine lithium carbonate, and d-amphetamine and l-amphetamine together with lithium. d-Amphetamine significantly decreased MHPG excretion. No significant change in MHPG was observed during administration of l-amphetamine or when d-amphetamine or l-amphetamine was given together with lithium carbonate. Six patients responded with behavioral activation and euphoria to d-amphetamine, and these patients tended to have lower baseline MHPG values in comparison to the nonresponders. Reductions in MHPG excretion during amphetamine administration were greatest in the patients with minimal behavioral responses to the drug, while some of the patients demonstrating more marked stimulant effects had elevated levels of MHPG during the amphetamine administration period. It is concluded that variable changes, including elevated levels of MHPG in the responders, might represent the contribution of amphetamine related changes in clinical state, including increased physical activity and the development of hypomania. 37 references. (Author abstract)

001730 Benkert, O.; Lucke, K. H. Psychiatrische Klinik der Universität, Nussbaumstrasse 7, D-8000 Munich 2, Germany /Effect of thyrotropin releasing hormone in comparison to placebo in depressive patients treated with imipramine./ Wirkung von Thyreotropin Releasing Hormon im Vergleich zu Placebo bei mit Imipramin behandelten depressiven Patienten. *Arzneimittel-Forschung* (Aulendorf). 26(6):1162-1164, 1976.

The combination of thyrotropin releasing hormone (TRH) and imipramine was studied in 30 patients with retarded depression in a placebo controlled trial. The 20 female and 10 male patients, 21 to 63 years old, average age 44.5 years, showed involutional depression in 7, manic-depressive psychosis, depressed phase in 15, and depressive neurosis in 8. All patients received 150mg/day imipramine for 20 days (75mg the first 3 days). In a double-blind procedure, half the patients received 40mg TRH orally b.i.d. and the other half received placebo b.i.d. for 14 days. Patients were rated on the Hamilton Depression Scale and the self-rating von Zerssen Scale. There was no significant difference in therapeutic effect or side-effects between the two groups. 9 references.

001731 Bennie, E. H.; Schiff, A. A. Leverdale Hospital, Glasgow, Scotland A comparison of amitriptyline and a fluphenazine/nortriptyline preparation in anxiety-depressive states. *Scottish Medical Journal* (Glasgow). 21(4):204-209, 1976.

Patients suffering from mixed anxiety/depressive reactions, referred to the outpatient department of a large psychiatric hospital, were treated with either amitriptyline tablets or fluphenazine with nortriptyline tablets for a 4 week period. The study utilized a double-blind, completely randomized design, and patients' progress was assessed by means of the Wing Present State Examination (PSE), the Wakefield Self-Assessment Depression Inventory, and a side-effects inventory. Both the symptom rating scales showed that purely depressive symptomatology improved significantly in each treatment group, but the patients' self-ratings showed that only fluphenazine/nortriptyline (f/n) produced a significant alleviation of anxiety symptoms and panic attacks. The patients receiving f/n rated themselves as significantly less irritable, as well as less anxious, after 4 weeks treatment, than those receiving amitriptyline. The PSE schedule did not differentiate between the two treatment groups, but self-rating, which is a

more sensitive method of eliciting drug effectiveness in patients suffering from mild psychiatric disorders, did demonstrate patient preference for f/n. Implications for compliance with treatment are suggested. 16 references. (Author abstract)

001732 Benson, Robert. 508 Med-Dent. Building, Seattle, WA 98101. Psychological stress as a cause of Lithium prophylaxis failure, a report of three cases. *Diseases of the Nervous System*. 37(12):699-700, 1976.

Three cases of psychological stress as a cause of lithium prophylaxis failure are discussed. The cases suggest that unresolved psychological conflict will precipitate relapse in an otherwise compensated patient on lithium prophylaxis. In the data presented, the stress is not internal neurotic conflictual stress, but tangible stress. It is concluded that psychotherapy be combined with lithium prophylaxis to effect a lower relapse rate than lithium prophylaxis alone. 7 references.

001733 Blazer, Dan G., II; Petrie, William M.; Wilson, William P. Dept. of Psychiatry, Montefiore Hospital and Medical Center, 111 East 210th Street, Bronx, NY 10467 Affective psychoses following renal transplant. *Diseases of the Nervous System*. 37(12):663-667, 1976.

Six patients who developed affective psychoses following renal transplantation are discussed. Each patient was treated, with careful management, with appropriate drug therapy or somatic therapy, including phenothiazines, tricyclic antidepressants, electroconvulsive shock and lithium carbonate. Results of this therapeutic approach were uniformly successful. The similarity of affective psychoses that developed in this patient population and previously described psychoses attributed to steroid therapy is noted. It is concluded that the affective psychosis, whatever its physiologic origins, is reversible even in the presence of the presumed etiologic agent. This appears to suggest that the affective disorder occurring with steroid administration is merely triggered by the hormone. 17 references. (Journal abstract modified)

001734 Brewer, Colin. no address If speed kills, tricyclics massacre. *World Medicine* (London). 11(12):37-42, 1976.

Evidence is presented to show that tricyclics are overprescribed, more dangerous than other types of antidepressants and of doubtful effectiveness. It is shown that while the incidence of suicide due to overdoses of tricyclics has increased (9% of suicides are due to tricyclics), admissions to hospitals for depression have increased also, and it is suggested that risks involved in the prescription of tricyclics are not balanced by increased success in treating depression. In addition, an overdose of tricyclics requires longer hospital stay and careful cardiac monitoring, and is seen as being much more dangerous than overdoses of other antidepressants. In addition, tricyclics have suicide potential. It is suggested that more restraint be used in prescribing tricyclics and that amphetamines be reconsidered as an effective and safer alternative method of treatment. 9 references.

001735 Brodie, N. H. no address Once daily administration of fluphenazine/nortriptyline preparation in treatment of mixed anxiety/depressive states. *Current Medical Research Opinion*. 4:346-352, 1976.

A study of 223 patients diagnosed as having mixed anxiety/depressive states was carried out to compare the effectiveness of treatment with a once daily tablet preparation containing fluphenazine plus nortriptyline, taken either at night or in the morning, with the same total daily dose taken as one

tablet 3 times/day. Patients were randomly assigned to one of the three drug schemes. Both the patients' self-ratings and the physicians' assessments showed that there were highly significant improvements in all three treatment groups over the 4 week period. Although there were no clinically important differences between improvements in the nighttime dose and the 3 times daily dose groups, there was a higher incidence of drowsiness and tablet defaulting among patients taking one dose. (Author abstract)

001736 Carroll, Bernard J.; Curtis, George C.; Mendels, Joseph. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Neuroendocrine regulation in depression. I. Limbic system-adrenocortical dysfunction.** Archives of General Psychiatry. 33(9):1039-1044, 1976.

The regulation of hypothalamopituitary/adrenal (HPA) function in depressed patients was studied by a midnight dexamethasone suppression test. By using an observation period of 24 hours postadministration of dexamethasone, a graded series of abnormal test responses was identified. Depressed patients show abnormal early escape from suppression rather than absolute resistance to HPA suppression by dexamethasone. With increasing severity of depression, this escape occurs progressively more early on the day after administration of dexamethasone. The abnormalities were strongly related to the presence of HPA hyperactivity before dexamethasone was given. The essential disturbance of neuroendocrine regulation in depression is a failure of the normal brain inhibitory influences on the HPA system. This disinhibition of HPA activity suggests that there is an abnormal limbic system drive on the HPA axis in primary depressive illness. 34 references. (Author abstract)

001737 Choi, Sin J.; Taylor, Michael A. Veterans Administration Hospital, Perry Point, MD 21902 **Effect of lithium on Ca^{++} -A.T.P.ase.** Lancet (London). No. 7994:1080, 1976.

In a letter to the editor, data were presented on the effect of lithium on calcium adenosine triphosphatase (Ca^{++} -A.T.P.ase) using red cell membrane fragments from 12 male and female subjects. The results of the assay system indicate that lithium has no effect on Ca^{++} -A.T.P.ase. Thus it seems that lithium does not have a direct effect on the Ca^{++} transport mechanism and the observed changes in plasma calcium in patients treated with lithium may reflect the pathophysiology of affective disorder rather than an interaction between Ca^{++} transport and the lithium ion. 6 references.

001738 Ciccone, M.; Giannovola, E. Casa di Salute Psichiatrica dell'O.C., Prospero Alpino, Marostica, Italy /**Use of doxepine in the various clinical forms of depression./ Application of doxepine in varie forme cliniche di depressione.** Rassegna di Studi Psichiatrici (Siena). 65(6):1232-1236, 1976.

Use of doxepine in 35 patients with various kinds of depression is described. Doxepine therapy lasted one month. All subjects showed ameliorative signs after this period, especially the neurotic and psychotic depressives. Results showed that doxepine is most successful in patients exhibiting depressive mood, anxiety, and somatic symptoms. The use of Aitken's Visual Analogue Scale (VAS), which scales the state of mind of the subject, is considered an important adjunct to the evaluation of treatment with this psychotropic drug. 13 references.

001739 Coppen, A. J.; Ghose, K. Neuropsychiatric Research Unit, MRC Laboratory Greenbank, West Park Hospital, Epsom, Surrey, England **Clinical and pharmacological effects**

of treatment with a new antidepressant. Arzneimittel-Forschung (Aulendorf). 26(6):1166-1167, 1976.

Org GB 94 (Tolvon, Tolvin), a new tetracyclic piperazine-azepino compound, was compared with amitriptyline in 39 psychiatric inpatients with primary depressive illness. The dose of Org GB 94 was 20mg t.i.d., and the dose of amitriptyline was 150mg/day. Both drugs were given for 6 weeks. The Hamilton Depression Scale was completed by a rater who did not know the drug used before treatment and at 2, 4, and 6 weeks of treatment. Both drugs were of similar antidepressant efficacy. Patients with endogenous depression and reactive depression responded equally well to Org GB 94. At 2, 4, and 6 weeks of treatment, patients on Org GB 94 had fewer side-effects than they had reported while taking no drug at all, while patients on amitriptyline had more side-effects than on no drug. The difference in side-effects between the Org GB 94 and the amitriptyline groups was significantly different at all three points in time. Org GB 94 produced no change in blood pressure response to i.v. tyramine, thus indicating that Org GB 94 in therapeutic doses in humans does not block amine uptake into peripheral noradrenergic neurons. 5 references.

001740 Coppen, Alec; Gupta, Ramesh; Montgomery, Stuart; Ghose, Karabi; Bailey, John; Burns, Bruce; de Ridder, J. J. MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Mianserin hydrochloride: A novel antidepressant.** British Journal of Psychiatry (London). 129:342-345, 1976.

Mianserin (Bolvidon) was compared with amitriptyline in 39 inpatients with primary depressive illness. Patients were assessed before and at 2, 4, and 6 weeks after beginning drug therapy on the Hamilton Rating Scale and on a side-effects inventory completed by the patient. There was no significant difference in therapeutic efficacy between the drugs. Endogenous and reactive patients responded similarly to mianserin. Amitriptyline had significantly more side-effects than did mianserin. There was no relationship between plasma level of mianserin and therapeutic outcome. 10 references.

001741 Dencker, S. J.; Johansson, R.; Lindberg, D. Goteberg, Sweden **Correlation between plasma level and clinical response in manic psychotics given high dose fluphenazine enanthate.** Acta Psychiatrica Scandinavica (Kobenhavn). Supplement 265:22-23, 1976.

A summary of a report on the correlation of plasma level of fluphenazine enanthate and manic behavior, given at a symposium on psychiatric prevention and crisis intervention held in June 1976 at Turku, Finland, is presented. Two male patients with manic psychosis given 250m and 750mg respectively, of fluphenazine enanthate were continuously monitored for plasma level of the drug, behavioral target symptoms, and extrapyramidal side-effects. The plasma examinations demonstrated a fluphenazine peak after 1 hour, followed by a plateau during the 1 week study, with maximum plasma levels between the 2nd and 5th days. The rating showed a rapid decrease of the manic symptoms in both patients and only slight extrapyramidal symptoms.

001742 Egata, Keisuke. Department of Neurology, Toyama Prefectural Chuo Hospital, Japan **Two cases of MDI depression where carbamazepine was especially effective.** Psychiatria et Neurologia Japonica (Tokyo). 78(2):174-175, 1976.

The effectiveness of carbamazepine in treating depression was discussed in a paper read at the 67th Northern Japan Psychoneurological Symposium, held Feb. 17, 1974 at

Kanazawa, Japan. Two cases of manic-depression where the tranquilizing effects of carbamazepine (Tegretol) were marked are reported. In one case the amplitude of the manic-depressive cycle was notably reduced. In both cases, their depression appeared before periods of euphoria, and their premanic personalities were of the tenacious character as described by Shimoda. Abnormal brainwave patterns were noted in only one of the patients.

001743 Filho, Helio Tavares. Centro de Estudos de Casa de Saude Santa Clara, Belo Horizonte, Brazil /Treatment of depression with butriptyline./ Depressao -- tratamento com Butriptilina. Revista Brasileira de Medicina (Rio de Janeiro). 32(7):513-515, 1976.

To test the efficacy of butriptyline hydrochloride in the treatment of depression, 20 patients were administered oral doses, 75 to 125mg daily, of the drug over a period of 2 to 4 months. Seventy percent found it effective enough to enable them to resume normal daily activities. Side-effects included somnolence, dryness of mouth and, in one case, nausea, but not of sufficient severity to warrant discontinuance of therapy. In 26.5% of the cases, severe symptoms of depression regressed totally. 9 references.

001744 Floru, Lucian; Czarny, G.; Tegeler, J. Rheinisches Landeskrankenhaus, Psychiatrische Klinik der Universitat, Bergische Landstrasse 2, D-4000 Dusseldorf, Germany /Double-blind comparative study with the new antidepressant viloxazine and imipramine in 50 hospitalized female patients./ Doppelblindstudie mit dem neuen Antidepressivum Viloxazin im Vergleich zu Imipramin bei 50 stationaren Patientinnen. Arzneimittel-Forschung (Aulendorf). 26(6):1170-1171, 1976.

Viloxazine (Vivalan) was compared with imipramine in a 4 week double blind trial in 50 female depressives with average age 52 years. After a washout period of 3 to 7 days, 25mg imipramine t.i.d. and 50mg viloxazine t.i.d. were given. Dosages were doubled after 1 week. Diagnoses of the patients were involuntal depression in 24, unipolar cyclothymia depressed phase in 8, reactive depressive psychosis in 10, bipolar cyclothymia depressed phase in 6, and latent psychosis in 2. Significantly more patients improved under viloxazine than imipramine, and significantly more patients became worse under imipramine. Viloxazine was slightly more rapid acting. There were fewer side-effects under viloxazine. Side-effects for each drug are listed. No abnormal laboratory values occurred. EEG results showed an improvement in 30% of the patients on both medications. The chemical structure of viloxazine is shown.

001745 Francis, A. F.; Williams, R.; Cole, E. N.; Williams, P.; Link, J.; Hughes, D. University Hospital of Wales, Cardiff, Wales The effect of clomipramine on prolactin levels -- pilot studies. Postgraduate Medical Journal (Oxford). 52(Suppl. 3):87-91, 1976.

Three pilot studies investigated the effect of clomipramine on prolactin secretion, both in the response to a single dose in normal Ss and in treated depressed patients with steady state blood levels. The relationship of prolactin levels to side effects was also examined in patients receiving clomipramine and comparisons were made with amitriptyline. Findings indicated that prolactin levels are not raised in depressed patients who are not on medication. A rise in serum levels following a single dose and treatment for 3 to 6 weeks was noted in patients whose pretreatment levels were abnormal, although the response was not as predictable as with other compounds such as chlorpromazine. Treatment with amitriptyline did not affect

prolactin secretion at all. It is concluded that clomipramine causes a fairly consistent and progressive increase in serum prolactin levels, in contrast with amitriptyline, which had no effect in patients comparable in clinical severity and in patterns of clinical improvement on treatment. An initial impression that side-effects might be related to prolactin levels following a single dose of clomipramine was not confirmed. Comment is made on these observations, focusing on possible cause for the higher clomipramine induced prolactin levels, as compared to amitriptyline, the drugs' side-effects, and stress effects on prolactin concentration. (Author abstract modified)

001746 Gallant, Donald M.; Simpson, George M. no address Depression: bhavioral, biochemical, diagnostic and treatment concepts. British Medical Journal (London). New York, Spectrum Publications, 1976. 351p.

New knowledge and concepts relating to depressive illness are presented in 11 chapters by different authors in a variety of psychiatric fields. Some of the topics dealt with are: blood levels of antidepressants, diagnosis of depression in the elderly and in children; recent progress in the genetics of depression; and recent biochemical, physiological, and psychopharmacological research on manic-depressive illness. Commentary and a synopsis of group discussion are included in each chapter.

001747 Geisler, A.; Bech, P.; Johannesen, M.; Rafaelsen, O. J. Department of Pharmacology, University of Copenhagen, 20, Juliane Mariesvej, DK-2100 Copenhagen, Denmark Cyclic AMP levels in cerebrospinal fluid in manic-melancholic patients. Neuropsychobiology (Basel). 2(4):211-220, 1976.

The concentrations of adenosine 3'5'-cyclic monophosphate (cyclic AMP) in cerebrospinal fluid (CSF) in manic melancholic patients were studied. Control groups were patients suffering from other psychiatric disorders as well as neurological and orthopedic patients. The results showed no difference between the various diagnostic groups, including melancholic versus manic patients, unipolar versus bipolar types. The severity of the affective states measured by rating scales showed no correlation to cyclic AMP levels in CSF. The cyclic AMP levels were apparently not influenced by electroconvulsive therapy or treatment with lithium, neuroleptics, or tricyclic antidepressants such as haloperidol, imipramine, amitriptyline, chlorprothixen, and perphenazine. 27 references. (Author abstract modified)

001748 Gerner, Robert H.; Post, Robert M.; Spiegel, Allen M.; Murphy, Dennis L. Section of Psychobiology, Adult Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20014 Effects of parathormone and lithium treatment on calcium and mood in depressed patients. Biological Psychiatry (Amsterdam). 12(1):145-151, 1976.

The effects of parathormone (PTH) on serum calcium levels and on self-rated and observer rated behavior were investigated in depressed patients undergoing lithium carbonate administration. Seven patients with bipolar or unipolar depression received PTH infusions while being treated with both placebo and lithium in a double-blind design. Parathormone produced the expected increase in serum calcium and decrease in serum phosphate in moderately and severely depressed patients, but did not appear to alter subjective or objective measures of mood. A lack of acute effect of PTH on depression may be due to a variety of factors including the short duration of the trial, the dose of PTH, the magnitude of the calcium change, or possible lack of effective change in central nervous system calcium. Other alternative explanations are proposed. 51 references.

001749 Glassman, A.; Shostak, M.; Kantor, S.; Perel, J. New York Psychiatric Institute, New York, NY **Plasma level of antidepressant drug and outcome: the state of the art.** *Journal of Psychiatric Research* (Oxford). 13(1):60-61, 1976.

In a summary of a paper read before the Psychiatric Research Society, New York, October 31 to November 1, 1975, data from a study of plasma level of the antidepressant imipramine and clinical outcome in a population divided into unipolar and bipolar groups is presented and contrasted with clinical outcome in a population of endogenously depressed patients. When the population is stratified (unipolar nondelusional and bipolars lumped together) to match a Scandinavian study which used nortriptyline, a relationship between plasma level and clinical outcome can be demonstrated, but the relationship is sigmoid rather than curvilinear as found in the Scandinavian study. Although the Scandinavian study used no further stratification, the imipramine study population was divided into unipolar and bipolar groups. Within the unipolar group, not only is there a relationship between outcome and blood level but there is also a relationship between outcome and sex. Because the males within this group both did better clinically and developed higher blood levels, it is not clear if their superior clinical response is attributable to their higher blood levels or to their sex. In order to clarify the interrelationship between sex, blood level, and clinical response, the unipolar population was analyzed in separate male and female samples. A significant relationship between clinical outcome and menstrual state in both female bipolar and unipolar nondelusional patients was observed. Male patients show no relationship between age and blood level. Average female steady state levels rise following menopause as does their recovery rate.

001750 Goodwin, Frederick K. Laboratory of Clinical Science, National Institute of Mental Health, Bldg. 10, 4S239, 9000 Rockville Pike, Bethesda, MD 20014 **The drug treatment of mood disorders: Part I. Diagnosis, biological basis of drug effects, and general principles of drug therapy in the affective disorders** (Unpublished paper). NIMH, Bethesda, MD, 1976. 46 p.

The diagnosis, biological considerations and treatment of mood disorders are presented and discussed. Among the general diagnostic considerations included are: 1) the depressive spectrum; 2) episode duration; 3) patterns of recurrence in affective illness (the unipolar/bipolar distinction); 4) the syndrome of mania; 5) differentiating affective disorder, schizoaffective disorder and schizophrenia; and 6) differentiating affective illness from organic brain syndrome. Biological theories of affective illness are discussed under the headings: 1) function of the amine neurotransmitter systems; 2) the biochemistry of the synapse; 3) effects of drugs on amine function at the synapse; 4) evolution of the amine theories of affective illness by the correlation of clinical observation with biochemical studies of drug effects; 5) problems and limitations in the amine hypothesis; and 6) synthesis of current views concerning the role of neurotransmitter amines in affective illness and in the effect of drugs. Among the general principles of therapy outlined are: 1) pretreatment evaluation of depression; 2) general indications for the drug treatment of depression; 3) hospitalization and electroconvulsive therapy; 4) the experimental approach to the drug treatment of depression; and 5) duration of treatment. 50 references.

001751 Jain, Mishrilal. Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228 **Neuropsychobiology of affective disorders: some methodological considerations.** *Neuropsychobiology* (Basel). 2(4):247-257, 1976.

Studies are reviewed which bring into question the biogenic amine hypothesis as a definitive neurochemical postulate of affective disorders. These studies have failed to provide a direct and specific causative relationship between biogenic amines and affective disorders. An overview of the diverse effects of antidepressant drugs also undermine current theories of the biology of depression. Methodological problems involved in past clinical and neuropsychopharmacological studies are described. It is hoped that future studies will use an integrated and multidimensional approach, both in terms of clinical and experimental design, in order to obtain a better understanding of the biological bases of mental disorders. 72 references.

001752 Jarvik, Lissy F. Veterans Administration Hospital, Brentwood, CA **Aging and depression: some unanswered questions.** *Journal of Gerontology*. 31(3):324-326, 1976.

The subject of aging and depression leaves many unanswered questions, and the lack of precise and universally accepted definitions (not to mention an inadequate nosology) further complicates the issue. Little is known regarding the differentiation of depressive illness from a melancholic response to the stressful aging process, and equally little regarding the natural history of depressions with onset in the teens, 20s, or 30s. Studies are focusing on biochemical and physiological aspects of depression, but at present biochemists suffer from the uncertainties of the clinicians, and the clinicians and geneticists from the limitations of the biochemists. However, despite uncertainties about the condition, several effective forms of therapy have been developed, ranging from a focus on the therapeutic milieu to the use of pharmacologic antidepressants (particularly lithium). Ultimately, the question remains: why are not all elderly persons suffering from depression? The answer may lie in the interaction of environment, life stresses, and the internal adaptive capacities of the individual. 9 references. (Author abstract)

001753 Kral, Vojtech A. University of Western Ontario, London, Ontario, Canada **Somatic therapies in older depressed patients.** *Journal of Gerontology*. 31(3):311-313, 1976.

While psychotherapy is the treatment of choice in neurotic situational depressions of older patients, it is not effective enough in endogenous bipolar or monopolar depressions of elderly. These respond better to somatic therapy, mainly pharmacotherapy, or, if necessary, ECT. Experience shows the aged endogenous depressions respond favorably to tricyclic antidepressants as well as to monoamine oxidase inhibitors, although the dosage may have to be kept lower than with younger patients. ECT, if necessary, is well tolerated and effective in aged patients. However, proper precautions have to be taken before this treatment is commenced. Patients with a history or signs of recent coronary thrombosis or decompensated heart failure should be excluded. Also, the number of treatments should be kept at a minimum. The individual treatments should be spaced farther apart and so called "intensive treatment" avoided. If an endogenous depression lasts for more than 2 years and does not respond to any other kind of treatment psychosurgery may have to be considered. Experience has shown that long-lasting, deep depressions of the aged can be helped by this method without any important personality change. 6 references. (Author abstract)

001754 Lambert, P. A. Hôpital de Bassens, Clinique de Bressieu, F-73011 Chambéry, France **Psychoanalytic aspects of the treatment of manic-depressive psychosis.** *Sur quelques aspects psychanalytiques des traitements de la psychose maniaco-dépressive.* *Evolution Psychiatrique* (Toulouse). 41(3):557-582, 1976.

The effects of psychopharmacological and physiotherapeutic treatment of intrapsychic processes, such as manic-depressive psychosis, are discussed. Complex reactions of patients with melancholia, repetitive behavior, narcissism, mania, and schizophrenia to antidepressants and lithium are discussed. The actions of certain chemical components of psychotropic and neuroleptic drugs on pathological behavior is still in question. It is concluded that the premorbid personality of the patient is the decisive factor in the eventual effect of the chemical drug rather than the particular illness or drug administered. 18 references.

001755 Lipman, Ronald S.; Covi, Lino. Clinical Studies Section, Psychopharmacology Research Branch, NIMH, Bethesda, MD 20014 **Outpatient treatment of neurotic depression: medication and group psychotherapy.** In: Spitzer, R., Evaluation of psychological therapies. Baltimore, Johns Hopkins University Press, 1976. (P. 178-208).

The efficacy of two medications (benzodiazepine and imipramine) and two types of psychotherapy (brief supportive contact and psychodynamically oriented group psychotherapy) were assessed in 149 depressed female outpatients. The most reliable main effects were related to medication, with imipramine favored over benzodiazepine and placebo in a 4 month active medication phase and a 12 month maintenance phase. No clinical differences were found between patients receiving group psychotherapy and those receiving individual supportive contact. However, interaction patterns between drug and psychotherapy suggested that the advantage for imipramine was more marked in minimal than in group contact. Placebo patients showed more improvement in somatic anxiety under group psychotherapy than under brief supportive contact. 26 references.

001756 Loo, Henri. Service Hospitalo-Universitaire de Sante' mentale et de Therapeutique, Paris, France **/Essay on determination of psychological effects of lithium./** Essai de determination des effets psychologiques du lithium. Evolution Psychiatrique (Toulouse). 41(3):583-593, 1976.

Psychological effects of long-term lithium treatment are discussed. Questions are raised concerning the psychological effect of biochemical normalization due to lithium, the placebo effect of lithium on the patient, and the effect of lithium on the quality of mental functions. A study was done of 30 patients, 20 of whom showed manic-depressive psychosis, and 10 dysthymic schizophrenia. They were asked: 1) if they felt normal since beginning lithium treatment; 2) if they considered themselves cured; 3) if the treatment should be continued; and 4) why they continued with lithium if they considered it useless. Results of long-term treatment with lithium and its action on the body are still inconclusive due to the patient's conviction of his dependency on it.

001757 Loosen, P. T.; Merkel, U.; Amelung, U. Psychiatrische Klinik, Universitat Munchen, Nussbaumstrasse 7, D-8000 Munich, Germany **/Combined sleep deprivation/chlorimipramine treatment of endogenous depression./** Kombinierte Schlafentzugs-/Chlorimipramin-Behandlung endogener Depressionen. Arzneimittel-Forschung (Aulendorf). 26(6):1177-1178, 1976.

Sleep deprivation combination with chlorimipramine therapy was compared to chlorimipramine therapy in 16 endogenous depressive patients who had been ill at least 3 months. The patients ranged in age from 21 to 59 years, with a mean age of 42.5 years. Chlorimipramine was given 150mg/day for 3 weeks. Patients were evaluated on the Hamilton Depression Scale and

the von Zerssen Self-Rating Scale 2 days before, and on days 1, 2, 3, 4, 5, 8, 10, 15, and 22 of therapy, between 9 and 10 a.m. The chlorimipramine/sleep deprivation group showed a rapid remission of symptoms, while slow remission was obtained in the chlorimipramine group. The difference between the two groups was statistically significant on the 4th day, but by the 8th day, the scores of the two groups had similar values. It appeared that some of the side effects of chlorimipramine (tremor, perspiration, tachycardia and orthostatic complaints) were milder following sleep deprivation. 11 references.

001758 Lugez-Renan, F. Faculte de Medecine, F-59000 Lille, France **/Contribution to the clinical study of a new neuroleptic: sultopride./** Contribution a l'etude clinique d'un nouveau neuroleptique: le sultopride. Semaine des Hopitaux (Paris). 52(7-8):423, 1976.

Sultopride was studied in 42 chronic psychotic patients. The drug was administered either i.m. or orally at a dosage of either 300 to 400mg/day or 800 to 1200mg/day. Results were very good in 23, good in 9, slight in 3, and null in 7. The target symptoms most affected were manic excitation, agitation, aggressivity, hallucinations, mental automatism, delirium, and autism. Side-effects were extrapyramidal symptoms, anxiety, and depression. Treatment with sultopride had to be interrupted in seven patients because of side-effects.

001759 MacKay, A. V. P.; Loose, R.; Glen, A. I. M. MRC Brain Metabolism Unit, Thomas Clouston Clinic, Edinburgh EH10 5LG, Scotland **/Effects of lithium therapy during pregnancy./** Labour on lithium. British Medical Journal (London). No. 6014:878, 1976.

A case report involving administration of oral lithium carbonate during the second and third trimesters of pregnancy to a manic-depressive young woman is reviewed. Detailed trans-placental analyses of the pharmacokinetics in this case indicated a close similarity of lithium concentrations in maternal, umbilical, and neonatal serum and confirmed that no placental barrier exists to the free diffusion of lithium ions. The high concentrations in amniotic fluid probably reflected fetal urinary excretion. Since lithium inhibits adenylate cyclase, the findings of no thyroid or parathyroid dysfunction in the newborn infant was surprising. Nurses observed that the baby was abnormally irritable while the serum lithium concentration was rapidly falling, and this behavioral abnormality may have resulted from withdrawing an agent to which the baby had been exposed for most of its intrauterine life. Further research is required before any general statement can be made regarding the safety of lithium therapy during pregnancy. Transmembrane electrolyte distribution in fetal mammalian brain tissue differs from that of the adult and thus the effect of lithium upon important ionic distributions in the developing brain should be further assessed. 4 references.

001760 Matussek, N.; Benkert, O.; Fidetzis, K.; Flach, D.; Hermann, H. U.; Kaumeier, S.; Kindt, H.; Kinzler, E.; Ruther, E.; Watzka, W. Psychiatrische Klinik, Universitat Munchen, Nussbaumstrasse 7, D-8000 Munchen 2, Germany **/Effect of the anthracene derivative danitracene (WA 335-BS) in comparison to amitriptyline in depressive patients./** Wirkung des Anthracenderivats Danitracen (WA 335-BS) im Vergleich zu Amitriptylin bei depressiven Patienten. Arzneimittel-Forschung (Aulendorf). 26(6):1160-1162, 1976.

Danitracene, a new tricyclic drug, was compared with amitriptyline in a double-blind study in 116 depressed patients. The patients, 91 females and 25 males, 30 to 60 years old,

average age 47 years, showed endogenous depression in 51, involuntary depression in 38, neurotic depression in 17, and reactive depression in 10. The patients were divided into two groups, with 59 patients receiving 1mg danitracene t.i.d. and 57 receiving 50mg amitriptyline t.i.d. Patients were evaluated on the Hamilton Depression Scale and the self-rating von Zerssen Scale. At the end of 20 days, 67.7% of the patients on danitracene and 66.7% of the patients on amitriptyline showed a 50% decrease on the Hamilton Scale, while 57% of the patients on danitracene and 51.8% of the patients on amitriptyline showed a 50% decrease on the self-rating scale. There was no difference in side-effects between the two drugs and there were no pathological laboratory findings. 6 references.

001761 Mendels, Joe. Depression Research Unit, VA Hospital (151E), Philadelphia, PA 19104 **Lithium in the treatment of depression.** *American Journal of Psychiatry.* 133(4):373-378, 1976.

Studies of lithium as an antidepressant are reviewed, the evidence that there might be a specific subgroup of patients for whom it is effective is evaluated, and a study is reported in which lithium was found to be effective for 13 of 21 depressed patients. It is concluded that there is convincing, although not conclusive, evidence for an antidepressant effect of lithium, and that only by identifying the subgroup of patients for whom it is effective can the continuing uncertainty surrounding lithium's role in affective disorder be resolved. A reevaluation of the relationship between mania and depression is suggested. 56 references. (Journal abstract modified)

001762 Mendlewicz, Julien. Institut de Psychiatrie, Hôpital Universitaire Brugmann, 4, place Van Gehuchten, B-1020 Brussels, Belgium **Lithium and genetic equipment.** *Lithium et équipement génétique. Evolution Psychiatrique (Toulouse).* 41(3):551-556, 1976.

The action of lithium in correcting genetically based mental illnesses such as schizophrenia and manic-depression, and its importance in psychopharmacology are discussed. The possibility of correcting the genetic anomaly causing manic-depression with lithium is examined in a study of 89 manic-depressive patients during a 48 month period at the Lithium Clinic of the Psychiatric Institute of New York. Results show that genetic makeup influences the rate of success of lithium treatment. It is concluded that studies of the action of lithium in manic-depressive psychosis are needed. 21 references.

001763 Messiha, F. S.; Erickson, H. M., Jr.; Goggin, J. E. Department of Pharmacology and Therapeutics, Texas Tech University School of Medicine, Lubbock, TX 79409 **Lithium carbonate in Gilles de la Tourette's disease.** *Research Communications in Chemical Pathology and Pharmacology.* 15(3):609-612, 1976.

The effect of lithium carbonate on Gilles de la Tourette's syndrome was studied in two males, aged 5 and 22 years old. Both patients received lithium carbonate in increasing doses to obtain a plasma Li concentration between 0.8 and 1.0 mEq/l. Other medications were discontinued for 7 days prior to administration of lithium. The target symptoms of involuntary motor acts, tics, involuntary sounds, and coprolalia were rated on a scale of 1 to 4. In both cases, symptoms responded to lithium carbonate when blood plasma Li levels stabilized in the 0.8 to 1.0 mEq/l range. Maximal symptoms reduction was noted after 3 weeks of Li therapy and has persisted to date. It is postulated that hyperactivity and/or hypersensitivity in the dopaminergic system is related to Tourette's syndrome and that lithium exerts its beneficial effects by modifying these parameters. 8 references. (Author abstract modified)

001764 Mikhail, A. R. Baylor College of Medicine, Waco, TX 76706 **Treatment of vaginismus by i.v. diazepam (valium) abreaction interviews.** *Acta Psychiatrica Scandinavica (Kobenhavn).* 53(5):328-332, 1976.

A new method of treatment of vaginismus by using intravenous diazepam abreaction interviews for anxiety and psychosomatic symptoms is reported. Four patients between the ages of 19 and 28 were interviewed. The duration of their main complaint varied from 6 months to 3 years. Three to six abreaction interviews were conducted; the maximum dosage of Valium used was from 20-30mg. All of these patients reported having successful intercourse after these interviews. Individual psychotherapy continued after the interviews on a weekly basis, and marital therapy on a monthly basis, for a period of 2 to 6 months. Three out of four women reported being orgasmic for the first time. This method of treatment of vaginismus is recommended as greatly beneficial. 7 references. (Author abstract)

001765 Mills, Ivor H. University of Cambridge Clinical School, Addenbrooke's Hospital, Cambridge CB2 2QQ, England **Amitriptyline therapy in anorexia nervosa.** *Lancet (London).* No. 7987:687, 1976.

In a letter to the editor, it is posited that the benefits of amitriptyline therapy in the treatment of anorexia nervosa were exaggerated in the report of research done by Needham and Waber (1976). In a previous study of anorexia nervosa it was found that while depression could be controlled by the administration of tricyclic antidepressants, some patients still required hospitalization, and varying degrees of persuasion by the medical and nursing staff were necessary before the patients gained any weight. It was concluded that these patients were better able to cope with social and academic pressures when maintained on tricyclics.

001766 Muller-Oerlinghausen, B.; Neumann, H.; Ruger, U. Psychiatrische Klinik, Freie Universität Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany **Study of the importance of neurotic psychological factors in the success of long-term lithium treatment.** *Untersuchung über die Bedeutung neurosenpsychologischer Faktoren für den Erfolg der Lithium-Dauerbehandlung.* *Arzneimittel-Forschung (Aulendorf).* 26(6):1181-1183, 1976.

Neurotic personality factors were studied in 20 female manic-depressive patients ranging in age from 31 to 60 years. The patients had been on lithium therapy for at least 1.8 years, with an average of 4.3 years. Five patients were receiving at least 75mg/day of a tricyclic antidepressant. Of the 20 patients, 11 were bipolar and 9 were monopolar. All patients were interviewed in depth by an interviewer who did not know the patient's treatment course and prognosis, and was seeing the patient for the first time. In addition, all patients took the Freiburger personality inventory. Results showed a rise in new drives and conflicts in 12 patients, and there were severe neurotic conflicts in 6 patients and moderate neurotic conflicts in 8. A total of eight patients showed an indication for psychoanalytically oriented psychotherapy. Thus, a subgroup of outpatients should be given psychotherapy in addition to long-term lithium therapy. 15 references.

001767 Neubauer, Harry; Bermingham, Peter. Psychiatric Unit, Royal United Hospital, Combe Park, Bath BA1 3NG, England **A depressive syndrome responsive to lithium: an analysis of 20 cases.** *Journal of Nervous and Mental Disease.* 163(4):276-281, 1976.

An analysis is made of a series of 20 patients seen over the past 4 years who have shown a dramatic improvement following the introduction of lithium carbonate to their therapy. The results indicate that these patients showed a consistent syndrome with the following features: 1) anergic endogenous depression; 2) positive family history in first degree probands; 3) obsessional personality traits and symptoms; 4) hypochondriasis and somatic symptoms; 5) failure to respond to previous antidepressant therapy with tricyclic compounds and monoamine oxidase inhibitors as well as electroconvulsive therapy. A previous study showed that one third of a series of psychotic depressives admitted to the Maudsley Hospital, London, also displayed obsessional symptoms and hypochondriasis. These patients, however, seemed to do as well with standard antidepressant treatment as a control group of psychotic depressives without obsessional features. However, in this series there was a 7% residue whose obsessional symptoms worsened, even after recovery from their depression. These patients represented approximately 3% of all psychotic depressives seen over the 4 year period. The mean age of onset of illness was 45.5 years, and this finding, coupled with the high incidence of psychotic depression in first degree relatives, indicates that these patients were suffering from psychotic depression modified by personality traits, rather than an atypical obsessional neurosis. The consistency of clinical features and specificity of response to lithium therapy appear to indicate that this is a clearly definable clinical syndrome worthy of further investigation. 12 references. (Author abstract)

001768 Novellone, M.; Debenedetti, M. Ospedale Civile di Asti, Divisione Neurologica, Asti, Italy /*Observations of the intravenous administration of sulphiride (Dobren).*/ Osservazioni sull'impiego della sulphiride (Dobren) per via venosa. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(2):529-534, 1976.

Sulpiride (Dobren) was administered intravenously to 81 patients, 15 to 76 years old. Patients, all hospitalized, suffered from depression, obsession, phobias, and other psychoses and neuroses. Good effect resulted in 65% of the subjects, mediocre results in 22%, no effect in 9.5% and deterioration in 3.5% of the subjects. Overall, the research was considered successful and it was concluded that both the absence of side-effects and the rapidity of action of sulphiride make it a most desirable drug to be used with these kinds of mental patients. 5 references.

001769 Ohman, Rolf; Walinder, Jan; Balldin, Jan; Wallin, Leif; Abrahamsson, Lars. Department of Psychiatry, University of Goteborg, Goteborg, Sweden *Prolactin response to electroconvulsive therapy*. Lancet (London). No. 7992:936-937, 1976.

Prolactin response to electroconvulsive therapy was investigated in nine patients with endogenous depression. Four patients undergoing minor gynecological surgery who had had the same type of intravenous anesthesia as the ECT group were studied as controls. After 15 min of ECT there was a 10 to 50 fold increase in serum prolactin in eight of the patients. The effects of anesthesia and surgery on serum prolactin in the controls were negligible. 14 references. (Author abstract)

001770 Paykel, E. S.; Tanner, J. Department of Psychiatry, St. George's Hospital, London SW 17, England *Life events, depressive relapse and maintenance treatment*. Psychological Medicine (London). 6(3):481-485, 1976.

Occurrence of life events was recorded in 30 recovered depressed women undergoing clinical relapse in a controlled trial of maintenance treatment with amitriptyline and psychotherapy, and in 30 matched patients who did not relapse. Overall, patients who relapsed experienced significantly more life events in the 3 months before relapse, and especially in the month immediately preceding it. Undesirable events were particularly implicated. Event rates prior to relapse were closely comparable in treatment subgroups, giving no evidence that differential stress was required to produce relapse. The findings reinforce previous studies indicating an overall relationship between life events of certain types and depression, but do not suggest that the beneficial effects of maintenance treatment are specifically protective against life stress. 12 references. (Author abstract)

001771 Priora, P. M.; Ollino, S.; Nanni, S.; Lombardi, F. Ospedale Psichiatrico San Giacomo, Alessandria, Italy /*Therapeutic proposal for involuntal depression.*/ In tema di depressioni involutive una proposta terapeutica. Rassegna di Studi Psichiatrici (Siena). 65(6):1257-1266, 1976.

Following a description of effects evaluation of action of noxiptiline (BAY 1521) and its rapid effect on different kinds of depression, a clinical trial of noxiptiline in 20 female patients, 60 to 78 years old, who had been hospitalized for 5 to 15 years, is described. Results showed the antidepressant was effective in 80% of patients with involuntal depression, and presented relatively few side-effects. Although the study results are highly positive, it is recommended that appropriate psychotherapy be administered concomitantly by trained hospital personnel. 11 references.

001772 Renfordt, E.; Busch, H.; Fahndrich, E.; Muller-Oerlinghausen, B. Psychiatrische Klinik, Freie Universitat Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany /*Study of a new antidepressant (viloxazine) with the help of time series analysis of videotaped interviews.*/ Untersuchung einer neuen antidepressiven Substanz (Viloxazin) mit Hilfe der Zeit-Reihen-Analyse TV-gespeicherter Interviews. Arzneimittel-Forschung (Aulendorf). 26(6):1114-1116, 1976.

Videotapes were made of 19 depressed patients, 6 males and 13 females, participating in a double-blind comparison of viloxazine and amitriptyline. Nine patients were given 300mg/kg viloxazine and 10 patients were given 150mg/day amitriptyline. Patient interviews were videotaped on the day before treatment, and on the 10th and 20th days of treatment. A 2 min excerpt was made of each interview for rating. The excerpts were rated by four psychiatrists who did not know the sequence of the video tapes. The psychiatrists rated the patients as severely, moderately, or slightly depressed. The tapes could easily be discriminated in terms of decreasing depression. Viloxazine seemed to have a quicker onset of action than amitriptyline. 5 references.

001773 Saletu, B.; Schanda, H.; Grunberger, J. Psychiatrische Universitätsklinik, Allgemeines Krankenhaus der Stadt Wien, Lazarettgasse 14, A-1097 Wien, Austria *The treatment of endomorphous and psychogenic depressions with a fixed combination of amitriptyline/flupenthixol (Lu 7410)*. International Pharmacopsychiatry (Basel). 11(2):109-128, 1976.

The clinical efficacy of a fixed combination of 10mg amitriptyline and 0.5mg flupenthixol (Lu-7410) was studied in 15 endomorphous and 15 psychogenic depressive patients. There was a lack of extrapyramidal side-effects as well as alterations in blood count, blood chemistry and ECG. A decrease in the Taylor anxiety score and increase in concentration was noted,

based on the AD test. 26 references. (Author abstract modified)

001774 Saran, Brij M.; Russell, Gerald F. M. Netherne Hospital, Coulsdon, Surrey, England **The effects of administering lithium carbonate on the balance of Na, K and water in manic-depressive patients.** *Psychological Medicine* (London). 6(3):381-392, 1976.

Eleven patients in remission from manic-depressive illness were studied by means of metabolic balances before and after the administration of lithium carbonate. Lithium (Li) caused a sharp diuresis of isotonic saline and a smaller excretion of potassium over the course of 2 days. During the subsequent 2 days there occurred a compensatory retention of sodium (Na), potassium (K), and water. These short-term changes were not associated with any significant alteration in the patients' mood. There was no significant and systematic retention of Na, K, or water over the 14 days of Li administration. The recovery of Li was measured simultaneously. During the first week only a proportion of the administered Li was recovered in the urine and feces, suggesting that a gradual distribution of Li throughout its body space was occurring. After the first week, nearly all the administered Li was recovered, indicating an equilibrium with an even distribution of the ion throughout its body space. This equilibrium was more complete at this early stage in those patients who had been given a smaller dose of lithium carbonate. 42 references. (Author abstract)

001775 Sathananthan, Gregory L.; Gershon, Samuel; Almeida, Manny; Spector, Neil; Spector, Sidney. Department of Psychiatry, NYU Medical Center, 550 First Ave., New York, NY 10016 **Correlation between plasma and cerebrospinal levels of imipramine.** *Archives of General Psychiatry*. 33(9):1109-1110, 1976.

The levels of imipramine hydrochloride and desipramine hydrochloride (desmethylinipramine) in the plasma and cerebrospinal fluid (CSF) in 11 depressed patients was measured. The oral doses correlated significantly with the plasma levels irrespective of different diagnostic categories. The CSF levels varied significantly. In the endogenous depressive group the CSF levels were significantly higher in responders as compared to nonresponders. The CSF levels of the nonresponders in the endogenous depressive group, and of both responders and nonresponders in the schizoaffective groups, were similar. 12 references. (Author abstract modified)

001776 Shering, Anne. no address **Psychiatric research in the MRC Brain Metabolism Unit.** *Nursing Times* (London). 72(38):1466-1467, 1976.

The work of the MRC Brain Metabolism Unit is psychiatric research, which focuses particularly on affective disorders such as bipolar manic-depression and unipolar depression is reported. Usual treatment includes electroconvulsant therapy and drug treatment with phenelzine, tranylcypromine, tryptophan, or amitriptyline. Patients who do not respond to standard therapy are treated with combinations of drugs or lithium carbonate. These patients also put on special dietetic regimens to forestall weight increase while on lithium. Other projects maintained by the unit include monitoring of the type and frequency of sleep movements in manic-depressive patients.

001777 Shopsin, Baron. Department of Psychiatry, New York Medical Center, New York, NY 10016 **Tryptophan and allopurinol in the treatment of depression.** *Lancet* (London). 1(7970):1189, 1976.

Under controlled conditions, 8 male patients with a history of gout received allopurinol combined with L-tryptophan for an acute recurrence of endogenous depressive episode. Results are interpreted with caution although all patients did show significant symptomatic improvement. Behavioral side-effects included a syndrome of anger, hostility, irritability, and temper outbursts in 2 patients, coinciding with a hypomanic state induced in another patient. Physical side-effects were infrequent and did not interfere with treatment response. The data justify controlled trials in depressed patients of both sexes. The role of serotonin in the symptomatic relief of endogenous depression is supported.

001778 Simpson, George M.; Lee, J. Hillary; Cuculic, Zarko; Kellner, Robert. Rockland Research Institute, Orangeburg, NY 10962 **Two dosages of imipramine in hospitalized endogenous and neurotic depressives.** *Archives of General Psychiatry*. 33(9):1093-1102, 1976.

Fifty one newly hospitalized depressed patients participated in a double-blind comparison of two dosage levels of imipramine hydrochloride. Improvement occurred with both dosage regimens. A greater and more consistent improvement was noted in the 300mg group than in the 150mg group. There were a few differences between the response of the endogenous and that of the neurotic depressives. A comparison of the response of deluded and nondeluded depressives indicated that the deluded patients responded less well than the nondeluded depressives, although half of the delusional group did respond to the treatment. 11 references. (Author abstract modified)

001779 Spring, Gottfried K. Department of Psychiatry, Case Western Reserve University, Cleveland, OH **The current role of lithium in the treatment of affective disorders.** *Psychosomatics*. 17(3):151-156, 1976.

The current role of lithium in the treatment of affective disorders is reviewed and a brief history of the therapeutic use of lithium for treatment of gout, epilepsy, heart disease and mental disorders is presented. Research comparing lithium treatment to treatment with phenothiazines has indicated that: 1) lithium is as effective in the treatment of acute mania as the phenothiazines, and that in cases of mild to moderate mania is preferable, as it is usually well tolerated and has fewer side effects; 2) although a combination of phenothiazines with lithium have been widely used in schizoaffective disorders, no rationale exists for this use, since chlorpromazine or phenothiazine are more efficacious and produce fewer complications; 3) use of lithium is contraindicated in schizophrenic patients; and 4) lithium is ineffective in the treatment of acute depression. Research on lithium prophylaxis undertaken by NIMH and the Veterans Administration is described. It was found that tricyclics are more effective in preventing bipolar depression although not significantly, and that they are significantly inferior to lithium in the prevention of mania. In the prevention of depression in unipolar illness, data seems to support the efficacy of tricyclics over lithium. Research into success of lithium treatment in affective disorders indicates that prognosis is best for patients who complete the first year of treatment without complications. Lithium toxicity and side-effects are briefly discussed. 36 references.

001780 Tafuna'i, S. S.; James, N. McI. Wakari Hospital, Dunedin, Fiji Islands **Severe mood disorders: a review.** *Fiji Medical Journal* (Suva). 4(6):382-386, 1976.

The causes, symptoms and treatment of severe mood disorders are reviewed. It is suggested that depression is caused by

an imbalance in brain monoamines and can also be affected by certain drugs depleting cerebral amines. Both physiological changes and psychological changes occur. Treatment of depression includes the use of one of the tricyclic group of antidepressants or monoamine oxidase inhibitors for at least 6 to 12 months. Manic-depressive patients require hospitalization and the administration of high doses of tranquilizers and lithium carbonate. 5 references.

001781 van den Burg, W.; van Pragg, H. M.; Bos, E. R. H.; Piers, D. A.; van Zanten, A. K.; Doorenbos, H. Department of Biological Psychiatry, Oostersingel 59, Groningen, The Netherlands **TRH by slow, continuous infusion: an antidepressant?** *Psychological Medicine* (London). 6(3):393-397, 1976.

In a double-blind crossover trial with placebo, a slow continuous infusion of thyrotropin releasing hormone (TRH) over a 4 hour period had no therapeutic effect on a group of 10 depressive patients. No difference was found between the depressive patients and a control group of normal subjects in thyroid stimulating hormone response, T3 resin uptake, T4 or free thyroxine index values as a consequence of the TRH infusion. 18 references. (Author abstract modified)

001782 Vendsborg, P. B.; Bach-Mortensen, N.; Rafaelsen, O. J. Psychochemistry Institute, Rigshospitalet, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark **Fat cell number and weight gain in lithium treated patients.** *Acta Psychiatrica Scandinavica* (Kobenhavn). 53(5):355-359, 1976.

Total amount of fat, fat cell size, and fat cell number were determined in 33 patients presenting manic melancholic disorders, under long-term lithium treatment. The weight gain during the treatment was estimated both by the patients themselves (questionnaire) and from their records. A positive correlation between fat cell number and weight gain was found whereas the fat cell size showed no correlation to weight gain. 19 references. (Author abstract)

001783 Wright, S.; Herrmann, L. Priory Day Hospital, Birkenhead, England **Double-blind attempt at comparison of effects of lofepramine and amitriptyline in outpatients with depressive clinical presentation.** *Doppelblindversuch zum Wirkungsvergleich von Lofepamin und Amitriptylin bei ambulant behandelten Patienten mit depressiven Zustandsbildern. Arzneimittel-Forschung* (Aulendorf). 26(6):1167-1169, 1976.

Lofepamine, a derivative of imipramine, was compared with amitriptyline in a double-blind study on depressive patients. Ratings were made at 1, 2, 3, and 8 weeks of treatment on the Hamilton Rating Scale for Depression, the Wakefield Self-Assessment Depression Inventory, and a scale for side-effects. The 40 patients, 34 females and 6 males, had a mean age of 46 years, and showed endogenous depression in 18, and reactive depression in 22. Predominating symptoms were severe depressive mood in 33, marked agitation in 26, and pronounced mental anxiety in 16. The dose was 70mg lofepramine or 50mg amitriptyline t.i.d. Of the 20 patients on each drug, 16 in the lofepramine group and 17 in the amitriptyline group completed the 8 week trial. No significant difference in clinical effects of the two drugs was noted. Endogenous and reactive depressives responded similarly. Side-effects occurred in seven patients on lofepramine and in nine patients on amitriptyline, and included tiredness, prolonged sleep, dizziness, difficulty in concentration, and dry mouth. 5 references.

10 DRUG TRIALS IN NEUROSES

001784 Becker, A. L. Johannesburg General Hospital, Johannesburg, South Africa **Oxprenolol and propranolol in anxiety states.** *South Africa Medical Journal* (Johannesburg). 50:627-629, 1976.

Fifty five male and female patients presenting with acute or chronic anxiety states were randomly assigned to one of two treatment groups - oxprenolol or propranolol - to test the anxiolytic efficacy of the two drugs. The duration of treatment was 14 days. Efficacy was assessed using a 19 item psychiatric rating scale, at the beginning of the trial and after 1 and 2 weeks. Both oxprenolol and propranolol improved the target symptoms of anxiety to a statistically significant extent, although there was no significant difference between them. Overall, both treatments improved the condition of over 90% of the patients to a moderate or marked degree.

001785 Chappa, H.; Levin, E.; Moizeszowicz, J. Hospital Melchor Romero, La Plata, Buenos Aires, Argentina **A new psychotropic for the treatment of anxious and depressive neuroses: Nomifensin.** *Tratamiento de las neurosis ansiosas y depresivas con un nuevo psicofarmaco: Nomifensin. Acta Psiquiatrica y Psicologica de America Latina* (Buenos Aires). 22(2):133-138, 1976.

The effect of Nomifensin (8 amino, 2-methyl-4-phenyl, 1,2,3,4-tetrahydroisoquinoline), a new psychotropic agent different from tricyclics and MAO inhibitors, was studied in patients with depressive anxiety syndromes. Thirty three patients (22 female, 11 male), average age 40 years, were studied for 5 weeks in an open trial. The educational and occupational levels of the sample were determined. Followup was carried out with Wittenborn Psychiatric Rating Scale, Hamilton Rating Scale for Depression, Zung Self-Rating Scale, and PEN Personality Inventory. No other drug was allowed to be taken along with Nomifensin, except for a benzodiazepine derivate for disturbed sleep. The average dose was 67mg per day. The changes in Hamilton and Zung scales were statistically significant, after the first week of treatment. Only the N scale of the PEN showed a before/after treatment significant difference. The correlation obtained between Zung and Hamilton Scales is discussed. The drug was shown to have thymoleptic action within the first week of treatment and an additional effect on anxiety symptoms, frequently associated with reactive depressions. 14 references. (Journal abstract modified)

001786 Cocchi, R.; Terribili, F. Centri di Igiene Mentale della Provincia di Pesaro e Urbino, Italy **Antidepressant action of clothiapine.** *Sull'attivita antidepressiva della clotiapina. Rivista Sperimentale di Freniatria* (Reggio Emilia). 100(3):749-759, 1976.

A trial of small doses of clothiapine in patients with adolescent depression is described. Clothiapine was used alone or in conjunction with an anxiolytic in 15 males and 1 female, 5 to 11 years old. The main aim of the research was to investigate the relationship between antidepressant effects and dosage of clothiapine. Favorable results were obtained in subjects suffering from character disturbances, scholastic difficulties, sleep and appetite disturbances, inhibition, and poor intellectual activity. It is concluded that the antidepressant action of clothiapine is effective in adolescents only at low dosage. Higher dosages of the drug often conceal the antidepressant action taking place in the patient. 29 references.

001787 Cohen, Jonathan; Gomez, Evaristo; Hoell, Noel L.; Kotin, Joel; Rickman, Edward E.; Roessler, Robert L. Depart-

ment of Medical Research, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Diazepam and phenobarbital in the treatment of anxiety: a controlled multicenter study using physician and patient rating scales.** *Current Therapeutic Research.* 20(2):184-193, 1976.

In a double-blind, multicenter study, two hundred and forty one patients with moderate or marked anxiety were randomly assigned to treatment with diazepam, phenobarbital, or placebo. Progress was evaluated at 1, 2, and 4 weeks by the physicians utilizing the Hamilton Anxiety Scale and by a global clinical evaluation, while patients completed the State Form of Spielberger's State-Trait Anxiety Inventory. Patients in the diazepam group improved more rapidly and to a greater degree than those given phenobarbital or placebo. These differences were statistically significant at all time periods. Improvement, not statistically significant, was greater in patients administered phenobarbital as compared to those given placebo. Results of this investigation, utilizing a common protocol and multiple rating scales to assess patient improvement, demonstrated the feasibility of conducting a large scale, multicenter study of patients with anxiety. 17 references. (Author abstract)

001788 Conway, Allan. Social Science Division, Herkimer County Community College, Herkimer, NY 13350 **An evaluation of drugs in the elementary schools: some geographic considerations.** *Psychology in the Schools.* 13(4):442-444, 1976.

The relationship between type of educational institution and the prescription of medication for elementary age children with behavioral problems was examined with questionnaire data obtained from school psychologists. Seven school psychologists in seven rural counties in New York State were asked how many students in grades K-6 received counseling for learning or behavioral problems. They were then questioned as to how many of this number were prescribed a drug as part of the corrective process. These findings were compared with information compiled by other researchers who studied urban based facilities and their therapeutic practices. It was hypothesized that there would be a positive correlation between geographic location and frequency of resorting to psychoactive drugs such as Ritalin as part of the therapeutic process. It was determined that rural systems have a much smaller percentage of children receiving psychoactive medications. Reasons suggested are that as population density increases there are a disproportionate number of complaints from teachers and school administrators, rural areas may be less transient and more homogeneous, and parent participation in the schools may be especially low in urban localities. 5 references. (Author abstract modified)

001789 de Silva, F. R. P.; Wijewickrama, H. S. de S. Department of Psychiatry, Southland Hospital, Invercargill, New Zealand **Clomipramine in phobic and obsessional states: preliminary report.** *New Zealand Medical Journal (Dunedin).* 84(567):4-6, 1976.

A preliminary report on the use of oral clomipramine in phobias and obsessional neuroses is presented. Twenty one patients, including 15 females and 6 males, aged 21 to 49 years, were treated. Fifteen had phobic symptoms and six showed obsessional neuroses. Nineteen of the 21 patients in the study had failed to respond to other treatment, but 20 benefitted from clomipramine. The effectiveness of clomipramine in the treatment of phobic and obsessional states is not proved, although the dramatic improvement seen in the present study suggests that it is effective. 8 references.

001790 Dereux, J.-F. Service de Neurologie, Hôpital Saint-Philibert, 10, rue de la Basse, F-59000 Lille, France / **Vagran 50: a situational antidepressant.** *Le Vagran 50: Un antidépresseur situationnel.* *Semaine des Hôpitaux (Paris).* 52(7-8):385-388, 1976.

Propizepine, a pyridobenzodiazepine, was studied in 30 patients suffering from depression. The 11 males and 19 females ranged in age from 15 to 72 years, with a modal number of the patients being between 41 and 50 years old. About 1/3 of the patients had endogenous depression (manic-depressive or involuntal) and 2/3 had nonpsychotic depression (reactive or neurotic). Using a global measure, results were satisfactory in 14 of the 30 patients. A total of 23 patients developed side-effects such as anticholinergic effects (dry mouth, sweating, tachycardia) or central effects (somnia, intoxication, insomnia, anxiety). The recommended dose of propizepine is 150 to 300 mg/day. Improvement was better in the nonpsychotic depressions, averaging 52%, whereas in the endogenous depressions, improvement averaged 33%.

001791 Escobar, Javier I.; Landbloom, Ronald P. University of Tennessee, Knoxville, TN 37916 **Treatment of phobic neurosis with clomipramine: a controlled clinical trial.** *Current Therapeutic Research.* 20(5):680-685, 1976.

A double-blind trial compared clomipramine to placebo in the treatment of nine phobic patients for a period of 6 weeks. Overall, patients on clomipramine showed a larger decrease in phobic symptoms than did patients on placebo. Differences in improvement reached statistical significance only at day 14 and favored clomipramine over placebo. It was the clinical impression that clomipramine has a positive therapeutic effect on patients with phobic neurosis. However, because of the small sample size, further controlled studies are needed to obtain decisive conclusions. 11 references. (Author abstract)

001792 Finnerty, R. J.; Goldberg, H. L.; Nathan, L.; Lowney C.; Cole, J. O. Outpatient Psychopharmacology Research Group, Boston State Hospital, Boston, MA **Haloperidol in the treatment of psychoneurotic anxious outpatients.** *Diseases of the Nervous System.* 37(11):621-624, 1976.

The clinical action and safety of haloperidol was investigated in psychoneurotic outpatients exhibiting anxiety, tension and agitation. Haloperidol was generally more effective than placebo in reducing anxiety and related symptoms. Twelve of the 39 patients were discontinued during the 4 week study due to deterioration of condition but 8 of the 12 were on placebo. Eight haloperidol patients reported side-effects not present prior to treatment; in three the symptoms were judged to be significant. Three patients showing clear "neuroleptic" side-effects, tremor or dystonia were all judged moderately or markedly improved. It is noted that while haloperidol clearly may be used to treat chronic or acute anxiety symptoms in neurotic outpatients, the drug does possess an unknown risk for eliciting tardive dyskinesia. Haloperidol may be less well tolerated by some patients who are on benzodiazepines but haloperidol lacks their potential for physical and psychological dependency. The risk benefit factors must be weighed by individual clinicians in prescribing for individual patients. 8 references.

001793 Guidotti, N.; Reitano, S.; Viana, P. Ospedale Psichiatrico Provinciale, Como, Italy / **Psychopathological problem of frustration of the "need to belong" in the light of three clinical cases.** *Il problema psicopatologico della frustrazione del "Bisogno di appartenenza" alla luce di tre casi clinici.* *Rassegna di Studi Psichiatrici (Siena).* 65(5):889-904, 1976.

The correlation between interpersonal communication and the need to belong were evaluated in three clinical cases to demonstrate how the individual is both frustrated and isolated when unable to communicate with his fellow man. The three subjects, males, 16, 34, and 74 years old, were not able to establish a meaningful dialogue with other individuals and consequently could not feel that they belonged to a group, because no interpersonal communication existed. On the basis of these clinical cases, it is suggested that some people can suffer from a defective ability to communicate; and even though given to neuroleptic or anxiolytic therapy, as these subjects were, they will continue to appear confused, isolated, incapable of orientating themselves in society, and show abnormal behavior. 20 references.

001794 Jovanovic, U. J.; Schulte, W. Universitäts-Nerven- und Poliklinik, Fuchsleinstrasse 15, D-8700 Würzburg, Germany /Polygraphic recording of sleep in endogenous depressive patients before and after treatment with amitriptyline-N-oxide./ Polygraphische Registrierungen des Schlafes bei endogenen depressiven Patienten vor und nach der Behandlung mit Amitriptylin-N-oxid. *Arzneimittel-Forschung (Aulendorf)*. 26(11):2106-2113, 1976.

Polygraphic sleep recordings were studied in 15 endogenous depressive outpatients. The seven males and eight females were 24 to 34 years old, with a mean age of 28 1/2 years. They were given placebo for the first 4 days, amitriptyline-N-oxide for the next 13 days, and placebo for the last 3 days. Recordings of EEG, EOG, EMG, EKG, and EDG were made on the first 7 nights and the last 6 nights while the patients slept. Under amitriptyline-N-oxide, latency of the first deep sleep and the first deep sleep and the first REM phase decreased, relative sleep duration increased, actual sleep duration was unchanged, frequency of awakenings during the night decreased, and duration of wakefulness after waking up during the night decreased. 55 references.

001795 Kalachev, B. P. Kafedra psikiatrii II Moskovskogo meditsinskogo instituta im. N. I. Pirogova, Moscow, USSR /An assessment of the effectiveness of autogenic training in comprehensive treatment of neurotic and psychopathic conditions./ Otsenka effektivnosti avtogennoy trenirovki pri kompleksnom lechenii nevroticheskikh i psikhopaticheskikh sostoyaniy. *Zhurnal Nevropatologii i Psikiatrii imeni S. S. Korsakova (Moskva)*. 76(11):1714-1719, 1976.

An evaluation was made of the connection between methods of treatment, especially autogenic, and regression of symptoms in 68 patients with neurotic and psychopathic conditions over a period of a year. Study methods included multiple regression, canonical correlation, and dispersion analysis. Autogenic treatment and aminazine were found to be most effective in hysteria, while autogenic training and amitriptyline were more effective in insomnia and inhibition. 13 references. (Author abstract modified)

001796 Miller, Phillip H. Tennessee Dept. of Mental Health & Mental Retardation, State Capitol, Nashville, TN 37219 Prescribing behavior altering drugs: dark clouds on the horizon. *Journal of the Tennessee Medical Association*. 69(10):720-721, 1976.

It is asserted that clinicians often rely too heavily on behavior altering drugs when other effective treatments are available. Despite the drugs' value many problems can arise: drugs affect a wide range of the client's behaviors, they do not help the client learn acceptable behaviors, and they can cause side-effects. A stringent documentation of problem behavior

and goal behavior enables easier evaluation of the drug treatment effectiveness and need for dosage variation. Such a documentation system is used at Greene Valley Developmental Center in Greeneville, Tennessee.

001797 Mills, Ivor H. University of Cambridge, Addenbrooke's Hospital, Cambridge, England The disease of failure of coping. *Practitioner (London)*. 217(1300):529-538, 1976.

The disease characterized by the failure of coping is analyzed in terms of cause, symptoms and treatment. The adaptations associated with coping are affected by the brain. Two processes are involved: 1) the redistribution of brain blood flow when reasoning problems beset the person; and 2) the elevation of the level of excitement or arousal which facilitates the effective use of the brain. Individuals with coping failure are divided into three groups: 1) inadequate coping ability; 2) excessive external challenges to coping; and 3) excessive internal drive. The clinical features of this syndrome include sleep disturbance, change in sexual processes, infertility, weight changes and compulsive behavior with depression being a constant component of the disease. The use of tricyclic antidepressants has been effective in preserving coping ability and restoring neuroendocrine normal states. 2 references.

001798 Murphy, J. Eric; Donald, J. F.; Molla, A. L. Northampton, England Mianserin in the treatment of depression in general practice. *Practitioner (London)*. 217(1297):135-138, 1976.

A double-blind comparative trial of imipramine, mianserin hydrochloride and a placebo was conducted. One hundred and five patients of mixed sex, aged 18-70 and in good physical health with a primary diagnosis of depression were administered identical tablets containing either 10mg mianserin hydrochloride, 25mg imipramine or placebo. Four tablets a day were administered for a period of 6 weeks. The results indicated that both mianserin hydrochloride and imipramine were significantly more effective than placebo after 2 to 3 weeks' treatment. No significant differences in antidepressant effect between mianserin hydrochloride and imipramine could be demonstrated nor were there any significant differences in side-effects among the three treatments. 8 references.

001799 Needleman, Herbert L.; Waber, Deborah. Department of Psychiatry, Children's Hospital Medical Center, Boston, MA 02115 Amitriptyline therapy in patients with anorexia nervosa. *Lancet (London)*. 2(7985):580, 1976.

The efficacy of amitriptyline in the management of six adolescent females, 11 to 17 years old, with anorexia nervosa is evaluated. All patients had severe aversion to food, at least 20% bodyweight loss, and cessation of menstruation. Amitriptyline was administered orally in individually determined doses. Patients consulted with a dietician daily and were encouraged to eat, but no systematic psychotherapy or behavior modification was used. Results reveal that all patients began to gain weight after 6 to 12 days of drug treatment and that weight gain was preceded by reported brightening of mood, increased warmth in extremities, and observed improvement in interpersonal relationships. Drug administration also improved other symptoms such as slow speech, immobility of the lower face, and parkinsonian like movement disorders. It is suggested that the positive response to amitriptyline may be a result of its general mood elevating effect. Prompt improvements in temperature regulation, motor behavior, speech, and appetite, however, are cited as evidence that this drug affected

hypothalamic catecholamine function, which has been found to play a role in the pathogenesis of anorexia nervosa. 3 references.

001800 Nielsen, N. P.; Reitano, S. Ospedale Psichiatrico Provinciale di Como, Como, Italy /Self-rating obsessional scale of Sandler and Hazari: preliminary observations./ La self-rating obsessional scale di Sandler e Hazari: osservazioni preliminari. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(2):475-489, 1976.

Clinical therapeutic effect of psychotropic drugs on obsessive psychoneurotics and normal subjects was evaluated by using the Sandler-Hazari self-rating obsessional scale. Subjects were divided into three groups, 24 with psychoneurotic obsession, 36 with personality obsession, and 30 normal individuals. The 60 obsessives were administered the Sandler-Hazari test before and after treatment with chlorimipramine, but the normals took the test only once. The 90 patients, aged 19 to 62, were equally divided into the groups according to sex, social status, and IQ. Conclusion was that the Sandler-Hazari test was useful in showing symptomatologic changes during psychotropic treatment and in discriminating between normal and obsessive subjects. However, the test showed a low validity for differential diagnosis between psychoneurosis and obsessive personality, and appeared more valid for psychotropic research than for psychopathology. 28 references.

001801 Pach, J.; Waniek, W. Rheinischen Landes- und Hochschulklinik für Psychiatrie, D-4300 Essen, Germany /Long-term tranquilizers: an alternative for practice./ Langzeit-tranquilizer -- eine Alternative für die Praxis. Arzneimittel-Forschung (Aulendorf). 26(6):1189-1190, 1976.

Fluspirilene was investigated in three studies involving 274 patients at dosages of 1 to 1.5mg weekly, and treatment lasting 4 to 7 weeks. Patients were rated by the Freiburger Personality Inventory, the Hampel Mood Scale, a complaint list, and the von Zerssen Self-Rating Scale. When compared with placebo in 26 patients over a 7 week period, fluspirilene was found to possess a definite tranquilizer effect. Patients showed improved mood, decreased depression, and remission of somatic complaints. Fluspirilene was then studied in 225 patients over a 12 week period. These patients also showed improvement in mood and remission of depression, tiredness, exhaustion, and somatic complaints. Finally, fluspirilene was compared with diazepam in an 8 week crossover study. Dosage of diazepam averaged 15mg/day. Diazepam was as effective as fluspirilene in relieving tension, but had no effect on depression. In addition, diazepam had an initial hypnotic effect, causing increased tiredness and exhaustion. Twelve patients on fluspirilene in the second study developed a fleeting akathisia, which responded to halving the dosage or to administration of biperiden. 8 references.

001802 Persson, G. Dept. of Psychiatry, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden Non-pharmacological factors in drug treatment of anxiety states. Acta Psychiatrica Scandinavica (Kobenhavn). 54(4):238-247, 1976.

Forty six outpatients with anxiety tension states participated in a study on the effects of anxiolytic drugs. After the first interview the subjects also filled in a questionnaire as to their expectations of treatment outcome and their experience of the first consultation, and the physicians made a prognostic evaluation. The relations between these three factors and background variables, as well as initial ratings and outcome as rated by the physicians at followup examinations after 2, 4,

and 8 weeks, were investigated. No relationship was found among expectations, experience, and prognosis. Less hopeful patients more often considered conflicts to be the exclusive cause of their disorder and they were rated higher on signs and on the variable difficulties in being with people. Patients with less favorable experience more often considered practical and economic difficulties to be a cause of their disorder. Single or divorced patients were more often judged to have a less favorable prognosis. More positive expectations and a favorable prognosis were to some extent related to a better outcome after 2 and 4 weeks and a favorable experience was to some extent related to a better outcome after 4 and 8 weeks. 10 references. (Journal abstract modified)

001803 Planche, R. Service de Psychiatrie, C.H.U., place Henri Dunant, F-63003 Clermont-Ferrand, France /Treatment of psychiatric emergencies./ Traitement des urgences psychiatriques. Semaine des Hopitaux (Paris). 52(7-8):383-384, 1976.

The diagnosis and treatment of acute psychotic delirium is discussed. A differential diagnosis must be made between a delirious bout, delirious reactivation of a schizophrenic process, manic crisis, manic-depressive psychosis, hysterical neurosis, reactive psychosis, puerperal psychosis, and drug abuse. A case report is given of a 25-year-old male who developed primary delirium. He was treated with 6 tablets/day of 400mg sulopride along with 3 tablets of the antiparkinson drug tropatepine for the first 3 days, followed by 4 tablets/day of sulopride for the next 4 days, and was released on the 8th day. This pharmacological regimen is recommended along with droperidol for sleep.

001804 Redmond, D. E., Jr.; Swann, A.; Heninger, G. R. Psychiatric Research Unit, Yale University, New Haven, CT 06510 Phenoxybenzamine in anorexia nervosa. Lancet (London). No. 7980:307, 1976.

Excessive noradrenaline activity is proposed as contributory to the ingestive components of some human appetite disorders and this effect may be diminished by using the alpha-adrenergic blocking agent, phenoxybenzamine. The hypothesis is supported by one case study of a woman with primary anorexia nervosa. Biological satiety mechanisms, the clinical case and animal research studies are discussed and considered supportive of this approach to related human appetite disorders. 11 references.

001805 Rickles, K.; Case, W. G.; Chung, H. R.; Morris, R. J.; Pereira-Ogan, J.; Rosenfeld, H.; Segal, A. Department of Psychiatry, University Hospital, Philadelphia, PA 19104 Lorazepam and diazepam in anxious outpatients: a controlled study. International Pharmacopsychiatry (Basel). 11(2):93-101, 1976.

The response of 134 anxious neurotic outpatients to lorazepam, diazepam, and placebo was assessed. Both active drugs produced significantly more symptom reduction than placebo. Lorazepam proved effective primarily in those patients who did not complain of sedation, and produced the greatest improvement in initially sicker patients. Sedation was significantly more disturbing to lorazepam treated patients than to diazepam treated patients. It was concluded that 3mg/day of lorazepam may be too high a dosage for mildly anxious patients, while 15mg/day of diazepam seems an appropriate dosage for mildly anxious persons but may be too low a dosage for highly anxious patients. 10 references. (Author abstract modified)

001806 Romildo Bueno, J.; Versiani Caldeira, Marcio V.; Rocha, A. V.; Mundim, F. D. Department of Psychiatry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil *Anti-anxiety effects of trazodone (a double blind study with diazepam and placebo).* Revista Brasileira de Medicina (Rio de Janeiro). 33(2):73-77, 1976.

A double-blind investigation of trazodone on 99 subjects, employing diazepam, a proven anxiolytic, and a placebo as controls, in the management of anxiety neuroses is presented. Trazodone was found to be equally effective as diazepam, while effects from the placebo were insignificant. In patients with glaucoma, prostatic hypertrophy or bladder symptoms, trazodone has the advantage of lacking anticholinergic or atropine like side effects. Hypnotic action, previously ascribed to diazepam and trazodone was found to be due more to the alleviation of the anxiety than to a sleep promoting action of the drug itself. In this series, headaches appeared in 10.3% of the subjects on trazodone treatment, though the direct relationship is not clear, as the finding conflicts with a very low incidence of headache in the previous literature. 16 references.

001807 Scharbach, H. Centre Hospitalier, Verdun, F-55107 France /*Trascor in psychiatry.* Le Trascor en psychiatrie. Psychologie Medicale (Paris). 8(6):945-950, 1976.

The effect on anxiety of oxprenolol, a beta-adrenergic blocker, was studied in 18 inpatients and a former inpatient with various psychiatric conditions. Diagnoses were obsessional neurosis in 5, hysterical neurosis in 4, hypochondriac neurosis in 1, schizophrenia in 4, and miscellaneous diagnoses in 5. The 9 men and 10 women ranged in age from 20 to 70 years, with mean age 40 years. Anxiety was mental in 9, somatic in 3, and mixed in 7. Somatic symptoms included palpitations, headache, digestive problems, perspiration, tremor, and dyspnea. The mean score on the Hamilton Scale was 36 before treatment, 18 during treatment, and 11 after treatment. There was a decrease in anxiety in 15 of 17 patients, and a decrease in depression in 13 of 15 patients. An obsessional neurotic experienced an improvement in his parkinsonism. Tolerance was satisfactory in 15 patients. 6 references.

001808 Snyder, Bruce D.; Kane, Maureen; Plocher, David. St. Paul-Ramsey Hospital and Medical Center, St. Paul, MN 55101 *Orphenadrine overdose treated with physostigmine.* New England Journal of Medicine. 295(25):1435, 1976.

The use of physostigmine in the treatment of orphenadrine overdose is reported in a letter to the editor. Orphenadrine citrate (Norflex) has been used as a muscle relaxant and has anticholinergic properties, but when ingested in large dosages can cause agitated delirium, hallucinations, delusions, paranoid thinking, and even death. The use of physostigmine in the treatment of anticholinergic overdose caused by other pharmaceuticals has been previously documented. Poison control centers should be aware that orphenadrine citrate is added to the list of intoxicants responding to physostigmine treatment. 2 references.

001809 Vanggaard, Thorkil. Department of Psychiatry, Rigshospitalet, Copenhagen, Denmark *Atypical endogenous depression: diagnostic criteria.* Acta Psychiatrica Scandinavica (Kobenhavn). Supplement 267:1-56, 1976.

An overview of atypical endogenous depression, aimed at contributing to the establishment of clinical diagnostic criteria, is presented. The five criteria are: 1) the primary gain; 2) the emotional secondary gain; 3) the interpersonal relationship and lack of neurotic symbiosis; 4) the unemotional mode of

presenting complaints; and 5) the reaction to antidepressant drugs. Twelve detailed case histories and an additional ten case summaries illustrate these five criteria. Differences between the atypical manic-depressives and patients with depressive neurosis are discussed. The turning of aggression upon the self is considered to be the key concept in the understanding of intrapsychic events in states of endogenous depression. Other topics discussed include: 1) the internal personality of the manic-depressive; 2) the interrelationship between psychological and somatic factors; and 3) the efficacy of antidepressants, particularly amitriptyline, in the treatment of atypical endogenous depression. 12 references.

001810 Versiani, Marcio; Bueno, J. R.; Mundim, F. D.; Da Silva, J. A. R.; Rocha, A. V. Mayer-Gross Clinic, Rua Gonzaga Bastos, 181 Vila Isabel, ZC 11, Rio de Janeiro 20000-RJ, Brazil *A double-blind comparison between loxapine and chlordiazepoxide in the treatment of neurotic anxiety.* Current Therapeutic Research. 20(5):701-715, 1976.

Fifty two neurotic outpatients with predominant anxiety were treated for 4 weeks with loxapine or chlordiazepoxide on a double-blind basis. Assessment based on the Hamilton Scale for Anxiety, Self-Rating Symptom Scale, and Clinical Global Evaluation showed significant improvement in most items and factors after the first week of treatment. Few significant differences arose from between group comparisons. Chlordiazepoxide appeared to be more effective in somatic symptoms. Abrupt suspension of medication did not induce withdrawal signs or symptoms in either group. The commonest side-effect in both groups was sleepiness. In general the two drugs were well tolerated. The laboratory tests performed did not yield abnormalities that could be considered drug related. The fact that few significant differences arose in the analysis is not considered "proof" that the two drugs are equivalent. The error involved in this type of reasoning, that of accepting a false null hypothesis, had a probability of about 80%. While it is concluded that the results of the present trial substantiate the similarity between loxapine and chlordiazepoxide as to efficacy and tolerance, the limitations involved in this type of reasoning are pointed out. 8 references.

001811 Vescovini, L. Istituti Ospedalieri Neuropsichiatrici S.Lazzaro, Reggio Emilia, Italy /*Double-blind clinical study of the anxiolytic action of a new agent: F.I. 6820 Brofoxine.* Studio clinico "Double Blind" sull'attività ansiolitica di un nuovo composto: F.I. 6820 Brofoxine. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(3):731-748, 1976.

Quantitative difference in anxiolytic action and tolerance of a new agent, F.I. 6820, (brofoxine), versus oxazepam was evaluated. A group of 20 patients, either hospitalized or outpatients, 17 to 76 years old, was studied. Patients were administered either brofoxine or oxazepam, in a 14 day double-blind study, after each subject had taken the Rating Scale for Anxiety States of M. Hamilton. The Hamilton test was repeated after 7 days and again after the 14th day of treatment. It was concluded that brofoxine possesses anxiolytic action comparable to oxazepam and is not only therapeutically effective but the patient suffers no side-effects from the drug. 5 references.

001812 Veyn, A. M.; Vlasov, N. A. Otdel patologiya vegetativnoy nervnoy sistema I. Moskovskogo meditsinskogo instituta im. I. M. Sechenova, Moscow, USSR /*Effectiveness of various methods in the treatment of sleep disorders, based on electropolygraphic data.* Effektivnost' razlichnykh metodov lecheniya narusheniy sna po dannym elektropoligrafii. Zhurnal

Nevropatologii i Pshikhiatrii imeni S.S. Korsakova (Moskva). 76(9):1379-1386, 1976.

The effectiveness of various methods of treating sleep disorder was evaluated using electropolygraph. A group of 111 patients with various forms of neurotic sleep disorder was given different variants of pharmacotherapy (calcium cyclobarbitol, eunocrin, elenium and diphenhydramine) and psychotherapy (hypnotic suggestion and autogenic training). Results indicated there is an increased activity of the awakening and activating systems in patients with such sleep disorders. A decrease in activating changes, evoked by pharmacotherapy and psychotherapy is accompanied by an improvement of the objective indices and regularly correlates with a subjective personal feeling of sleep. Optimal conditions for the various methods of treatment are presented, and principles for differentiated therapy are advanced. 20 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

001813 Aden, Gary C. Vista, Hill Hospital, 3 North Second Avenue, Chula Vista, CA **Lithium carbonate versus E.C.T. in the treatment of the manic state of identical twins with bipolar affective disease.** *Diseases of the Nervous System.* 37(7):393-397, 1976.

Identical twins suffering from a manic state and a depressive state were alternately treated with lithium carbonate and electroconvulsive therapy, respectively. Data are presented suggesting that the therapeutic and maintenance doses of lithium carbonate required for both twins are similar. Twin A received lithium carbonate from the inception of the author's experience with treating both twins under controlled conditions. Twin B received lithium carbonate during his second illness only 2 years after he had received electroconvulsive therapy. It is suggested that lithium carbonate effectively prevents recurrent manic illness, but electroconvulsive therapy may enhance occupational adjustment during normally expected remission periods and may further shorten the time required in the hospital for the treatment of manic illness. Twin A did not undergo an expected psychotic decompensation, as might have been expected prior to the use of lithium carbonate, while twin B did undergo a psychotic decompensation. 6 references. (Author abstract modified)

001814 Ballard, Joyce E.; Boileau, Richard A.; Sleator, Esther K.; Massey, Ben H.; Sprague, Robert L. Texas Eastern University, Tyler, TX **Cardiovascular responses of hyperactive children to methylphenidate.** *Journal of the American Medical Association.* 236(25):2870-2874, 1976.

Heart rate, blood pressure, and oxygen consumption were measured in 27 hyperactive children during rest, exercise, and recovery, first taking placebo and then taking methylphenidate hydrochloride. Half were measured first taking the drug and half first taking the placebo. Drug and placebo ECGs were recorded on 12 of the subjects. Oxygen consumption did not change, but heart rate and blood pressure increased significantly with methylphenidate therapy. There was a significant correlation between size of dose in mg/kg and increase in heart rate and blood pressure. No evidence of the development of tolerance to these drug effects was found in children who had been taking methylphenidate from 2 months to more than a year; no ECG changes other than tachycardia were seen. It is concluded that methylphenidate used in the treatment of hyperactivity is not contraindicated in the physician uses modest doses, monitors to find the child with excessive pres-

or responses, and terminated administration of medication as soon as clinically feasible. 15 references. (Author abstract modified)

001815 Bazhin, A. A. Leningradskiy oblastnoy psikhonevrologicheskoy dispensar, Leningrad, USSR **Experience in the treatment of alcoholic patients with chlorazepate in combination with rational psychotherapy.** *Opyt lecheniya bol'nykh alkoholizmom kloratsinom v sochetanii s ratsional'noy psikhoterapiyey.* *Zhurnal Nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva).* 76(6):909-911, 1976.

Chlorazepate, exerting a central cholinergic and adrenergic effect, was used in combination with individual rational psychotherapy during outpatient treatment of 68 alcoholic patients to arrest the withdrawal syndrome and suppress a morbid attraction to alcohol. The treatment was effective in 2/3 of the treated patients. 17 references. (Author abstract modified)

001816 Bech, P. no address **The effect of lithium in Meniere's disease.** no title. *European Journal of Clinical Pharmacology.* 10(5):331, 1976.

The effect of lithium administered for 6 months was investigated in patients with Meniere's disease in a double-blind, placebo controlled study. The lithium dose was adjusted every 2 weeks to maintain a serum level of 0.7 to 1.0 mmol/L. Subjects were within the normal range of Beck's depression scale and Marke-Nyman's temperament scale. Results reveal that lithium did not influence simulated driving or effect scores on either of the two rating scales. Side-effects of long-term lithium administration were tremor and increased thirst. (Journal abstract)

001817 Benedek-Jaszmann, L. J.; Hearn-Sturtevant, M. D. Department of Obstetrics and Gynecology, Regional Protestant Hospital, Bennekom, The Netherlands **Premenstrual tension and functional infertility: aetiology and treatment.** *Lancet (London).* No. 7969:1095-1098, 1976.

The value of bromocriptine, a prolactin suppressing drug which is effective because it is a long-acting dopaminergic agonist, in treating premenstrual tension and functional infertility was assessed in 17 women. Six received bromocriptine (CB 154) and placebo in a double-blind crossover manner. Five became pregnant and 10 who completed two cycles showed significant improvement in somatic symptoms and mood with the drug. Prolactin concentrations were suppressed. In 34 women with premenstrual symptoms, who had been warned of possible increased fertility, bromocriptine administered 2.5 mg twice daily from the 10th day of the cycle for 1 to 11 months gave marked or complete relief. A group of 45 women attending an infertility clinic took the same dosage for 186 cycles, and 23 became pregnant, two had marked relief, and 20 had complete relief from symptoms. The effectiveness of the drug may be due to suppression of prolactin concentrations, which appears to play a major role in premenstrual syndrome. 17 references. (Author abstract modified)

001818 Bjorkqvist, S.-E.; Isohanni, M.; Makela, R.; Malinen, L. Department of Physiology, University of Turku, SF-20520 Turku 52, Finland **Ambulant treatment of alcohol withdrawal symptoms with carbamazepine: a formal multicentre double-blind comparison with placebo.** *Acta Psychiatrica Scandinavica (Kobenhavn).* 53(5):333-342, 1976

One hundred male outpatients were treated for alcohol withdrawal symptoms with either carbamazepine or placebo in a double-blind, multicenter trial carried out at five Finnish A

clinics (alcoholism treatment centres) in different parts of the country. In both the carbamazepine and the placebo groups two thirds of the patients completed the seven day treatment successfully, and the final treatment results were considered equally good in both groups. However, the withdrawal symptoms, especially the sleep disturbances, subsided faster in the carbamazepine group than in the placebo group. The change in the total symptom score from the first day of treatment to the second was significantly greater in the carbamazepine group than in the placebo group. The patients' ability to work improved significantly faster in the carbamazepine group. 25 references. (Author abstract)

001819 Boshes, Louis D. Abraham Lincoln School of Medicine, University of Illinois Medical Center, Chicago, IL. **Gilles de la Tourette's Syndrome.** American Journal of Nursing. 76(10):1637-1638, 1976.

The case of a boy, age 14, with Gilles de la Tourette's Syndrome is described. He was placed on Haldol (haloperidol), which first produced a mild improvement and within a matter of weeks there was considerable improvement. Haldol is unusually effective in this syndrome, but numerous side-effects are reported. For patients who do well on Haldol it is hoped they also will be able to stop the medication for a certain length of time. The syndrome may be self-limiting, but it can be recurrent. An overview presents this illness as probably of both organic and/or inorganic origin, although it also may result from emotional stresses and strains in infancy or in childhood, such as removal of teeth or tonsils, birth of siblings, starting school, automobile accidents, parental quarreling, etc. Diseases which have been considered etiologic include measles, mumps, chicken pox, whooping cough, scarlet fever, encephalitis and chorea. Some postmortem examinations have revealed changes in the basal ganglia of the brain, and other reports support organic involvement of the central nervous system. 7 references.

001820 Butler, Robert N. 3815 Huntington Street, N.W., Washington, DC 20015 **Public interest report no. 19 -- the overuse of tranquilizers in older patients.** International Journal of Aging & Human Development. 7(2):185-187, 1976.

The overuse of psychoactive drugs in the treatment of elderly patients is discussed. It is recommended that guidelines for the use of psychoactive drugs, particularly for the elderly, be set for the following reasons: 1) psychotropic drugs are prescribed as for the convenience of others as for any benefit to the patient; 2) drugs often are substituted for comprehensive treatment; 3) drugs are often prescribed without consideration of long-term or short-term complications; 4) steroids can produce organic brain disorders as well as hypomania and depression; and 5) tranquilizers and hypnotics can cause tardive dyskinesia.

001821 Capstick, N.; Pudney, Helena. Graylingwell Hospital, Chichester, Sussex, England **A comparative trial of orphenadrine and tofenacin in the control of depression and extrapyramidal side-effects associated with fluphenazine decanoate therapy.** Journal of International Medical Research (Northampton). 4(6):435-440, 1976.

A double-blind, crossover trial involving 24 patients receiving fluphenazine decanoate was designed to compare the effects of orphenadrine hydrochloride and its major metabolite, tofenacin hydrochloride, on the Parkinsonian side-effects and depression occurring during fluphenazine decanoate therapy. It was found that both drugs exerted an adequate control on the Parkinsonian side-effects, but there was no significant dif-

ference between their effects. Orphenadrine, however, was shown to be significantly superior in the control of the depressive side-effects. 8 references. (Author abstract)

001822 Cavenar, Jesse O., Jr.; Maltebie, Allan A. Duke University Medical Center, Durham, NC **Another indication for Haloperidol.** Psychosomatics. 17(3):128-130, 1976.

Clinical trials of the uses of haloperidol for schizophrenic disorders, hallucinations, psychoneurotic conditions, organic brain syndromes, Gilles de la Tourette syndrome, the manic phase of manic-depressive illness, stuttering and as a potentiating agent of narcotic effects are briefly reviewed. Two case histories are presented in which haloperidol was used for pain relief in carcinoma. It was found that haloperidol used either with small doses of narcotic or alone provided effective pain relief. It is not known whether this effect is in part attributable to the correction of a severe psychiatric disturbance and the consequent relief of psychogenic pain; however, invariably, haloperidol provided significant relief of organic pain in malignant cases. 22 references.

001823 Coleman, Lee; Solomon, Trudy. no address **Big brother knows best.** Psychology Today. 10(6):85-88, 1976.

Through the state's increasing reliance on the legal doctrine of *parens patriae*, or the state as parent, the state has been making therapeutic interventions in the lives of wayward youths, the mentally disturbed, drug addicts and convicts considered too disordered to act on their own behalf. Such intervention is deemed to be not treatment, but legal punishment in disguise. The crucial issue is stated to be not whether the individual is suffering from a medical disease or is instead experiencing a "problem in living", but whether the individual has given prior consent. Without such consent the courts have ruled that medical treatment becomes criminal assault. The right to treatment conveys neither privilege nor immunity. It is contended that this right is instead being used to justify and further extend state interference when it is not wanted. The unjustified but expanding use of preventive psychiatry is manifested through Early Periodic Screening Diagnosis and Treatment, administered by the U.S. Department of Health, Education, and Welfare, which attempts to monitor the physical and mental health of every child of welfare mothers, and the U.S. Justice Department's attempt to develop a system of screening to spot potentially aggressive individuals. In addition, the increasing mandatory use of mind controlling drugs, such as lithium carbonate or the phenothiazines, by outpatient psychiatric treatment centers is described. 6 references.

001824 Coper, H.; Kanowski, S. Institut für Neuro-psychopharmakologie der Freien Universität Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany **Do geriatric drugs work? Wirken Geriatrika? Arzneimittel-Forschung (Aulendorf).** 26(6):1027-1028, 1976.

The discussion of a workshop on geriatric drugs is summarized. A distinction is made between prophylactic geriatric drugs and therapeutic geriatric drugs. Geriatric drugs include vitamins, hormones, and drugs which increase oxygen and glucose utilization in the brain. The difficulties in clinical drug trials in geriatric patients are considered, and this is followed by a discussion of the use of placebo controls. 13 references.

001825 Deberdt, R. Poperingeweg 10, B-8900 Ieper, Belgium **Pipamperone (Dipiperon) in the treatment of behavior disorders: a large-scale multicentre evaluation.** Acta Psychiatrica Belgica (Bruxelles). 76(1):157-166, 1976.

To investigate the efficacy of pipamperone (Dipiperon) in mental retardates as well as in patients with a normal I.Q., 188 patients showing behavior disturbances were administered pipamperone solution or tablets for four weeks. The doses were gradually increased until optimal effect was reached. It was found that nearly all 17 items of a behavior rating scale had improved very significantly by the end of the fourth week. Moreover pipamperone proved to be superior to previous treatments in most of the patients who had been treated with other psychotropic agents before. It can therefore be concluded that pipamperone either as tablets or as solution is a maniable tool in the treatment of aggressive and psychopathic behavior disorders both in mental retardates and in patients with a normal I.Q. 9 references. (Author abstract modified)

001826 Drymiotis, A.; Korenyi, C.; Whittier, John R. Creedmoor Institute for Psychobiologic Studies, Creedmoor Psychiatric Center, Queens Village, NY 11427 **Mesoridazine in Huntington's disease (chorea): effect on weight, dyskinesia, and mental function.** *Current Therapeutic Research*. 20(3):300-307, 1976.

A single-blind placebo controlled test study was designed to confirm a report of unusual weight gain in patients with Huntington's disease (chorea) treated with mesoridazine. Observations on six patients included a battery of clinical and laboratory tests, and a newly developed quantitative measure (cineismography) for abnormal involuntary movements. Weight gain occurred in only two patients. The severity and frequency of chorea diminished in two patients. According to the usual course of Huntington's disease, deterioration in general condition continued in four patients without apparent relationship to mesoridazine. Some decrease of depression was noted in the six patients. It is concluded that mesoridazine has no special pharmacological effect on the loss of weight characteristic of Huntington's disease. A possible relationship between the propensity for producing pharmacological parkinsonism and efficacy in the treatment of Huntington's chorea is discussed. 9 references. (Author abstract modified)

001827 Frith, C. D.; Johnstone, Eve C.; Joseph, M. H.; Powell, R. J.; Watts, R. W. E. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex, England **Double-blind clinical trial of 5-hydroxytryptophan in a case of Lesch-Nyhan syndrome.** *Journal of Neurology, Neurosurgery, and Psychiatry* (London). 39(7):656-662, 1976.

A double-blind clinical trial of 5-Hydroxytryptophan (5-HTP) treatment in 6-year-old boy of Lesch-Nyhan syndrome showing compulsive self-mutilation, athetoid movements, and characteristic clinical biochemical picture is reported. 5-HTP or placebo was administered for 7 fortnightly treatment blocks. 5-HTP produced a significant reduction of athetoid movement and a sedative effect but did not improve the patient's mood or reduce self-mutilation. 25 references. (Author abstract modified)

001828 Gilbert, John C. Department of Pharmacology, University of Aberdeen, Aberdeen AB9 2ZD, Scotland **Psychological medicine: drugs used in psychological medicine: pharmacological basis of treatment.** *British Medical Journal* (London). No. 6014:882-884, 1976.

Possible mechanisms of action and pharmacological considerations that are necessary in selecting specific psychotropic drugs are reviewed. The difficulties of confidently postulating one mechanism of action are emphasized. In cases of depression, monoamine oxidase inhibitors and tricyclic antidepressants are most widely used, while the benzodiazepines

have become popular in treating anxiety states. Chlorpromazine and other phenothiazines are prominent in treating schizophrenia because of their dramatic effect in controlling aggression and in stabilizing mood. Disulfiram is most commonly used in managing alcoholism, and barbiturates, mild tranquilizers, and antidepressants may be used to alleviate insomnia. Clinical and preclinical studies reveal the problems involved in obtaining exact reasons for effectiveness and mechanisms of action of these compounds.

001829 Gorodilova, Ye. P. Izhevskaya klinicheskaya psikiatricheskaya bol'nitsa, Izhevsk, USSR **Effectiveness of therapeutic methods in atherosclerotic psychoses and some indices in the hemocoagulation system.** *Effektivnost' metodov terapii ateroskleroticheskikh psikhovozov i nekotorye pokazateli sistemy gemokoagulyatsii.* *Zhurnal Nevropatologii i psikiatrii imeni S. S. Korsakova* (Moskva). 76(6):911-916, 1976.

A study of 127 patients with atherosclerotic psychoses established a substantial increase in some indices in the hemocoagulative system after age 50 and in pronounced cerebral and systemic atherosclerosis. Anticoagulant therapy was most effective in cases of cerebrasthenic affective syndromes and in conditions of altered consciousness. In cases of hallucinatory delusional syndromes and dementia, a combination of anticoagulants with psychotropic and antisclerotic preparations was more effective. Anticoagulant therapy normalizes or decreases the indices in the hemocoagulative system, and may therefore be considered as pathogenic. 16 references. (Author abstract modified)

001830 Herrschaft, H. Neurologische Klinik und Max-Planck-Institut für Hirnforschung, D-5000 Köln-Merheim, Germany **Therapy of cerebral ischemia.** *Die Therapie der cerebralen Mangeldurchblutung.* *Nervenarzt* (Berlin). 47(11):639-650, 1976.

An overview of the therapy of cerebral ischemia is presented. Since 1965, 364 patients with cerebral ischemia and manifesting such symptoms as hemiparesis, hemihypesthesia, aphasic disturbances, and scotoma were tested before and after the administration of various vasoactive pharmaceuticals. The pharmaceuticals effecting a decrease of cerebral blood flow were theophylline ethylenediamine, hydroxyethyltheophylline, and oxyethyltheophylline, xanthinol/niacinate, betapyridylcarbinol, raubasine, and naphthydrofuryl. Drugs having no influence on cerebral blood flow are: levalose, hydergin, dihydroergotamine, proxazol, bencyclan, hexobendin, and nicergolin. The following produced a slight increase in cerebral blood flow in the gray matter: centrophenoxine, Solcoseryl, and pyridoxin. The effects of the following are discussed extensively: the theophyllines, nicotinic acid derivatives, ergotamines, raubasine and hexobendin. At the present time no vasoactive preparation is known to achieve a statistically significant long-term improvement of cerebral ischemia. 106 references.

001831 Hoehn, Margaret M.; Crowley, T. J.; Rutledge, C. O. Department of Neurology, University of Colorado Medical Center, Denver, CO **Dopamine correlates of neurological and psychological status in untreated Parkinsonism.** *Journal of Neurology, Neurosurgery, and Psychiatry* (London). 39(10):941-951, 1976.

The relationship between free dopamine excretion and the severity of motor abnormalities and psychological abnormalities in 37 untreated Parkinsonian patients was studied. Significant positive correlations were found between decreased excretion of free dopamine (DA), Minnesota Multiphasic Personality Inventory (MMPI) scores indicative of schizophrenic

like thought disorder, and severity of all Parkinsonism signs except tremor. It is suggested that abnormalities of DA metabolism could underlie the psychological abnormalities as well as the motor abnormalities of Parkinsonism. However, reevaluation of several patients after therapy with L-dopa showed significant improvement in each neurological parameter but no improvement in psychopathology. 52 references. (Author abstract modified)

001832 Hughes, John R.; Williams, James G.; Currier, Robert D. University of Mississippi Medical Center, 2500 N. State St., Jackson, MS 39216 **An ergot alkaloid preparation (Hydergine) in the treatment of dementia: critical review of the clinical literature.** *Journal of the American Geriatrics Society.* 24(11):490-497, 1976.

A critical review is presented of 12 clinical trials with Hydergine (a hydrogenated ergot alkaloid preparation) in the treatment of senile dementia. Qualitative and quantitative comparisons of improvement in symptoms showed that Hydergine consistently produced statistically significant improvement in 13 symptoms associated with dementia. However, because of the small magnitude of the improvement and the absence of indications of long-term benefit, Hydergine would seem to be of minor value in dementia therapy. Further research with better methodology and design might lead to a different conclusion. 24 references. (Author abstract)

001833 Kesson, C. M.; Gray, J. M. B.; Lawson, D. H. Medical Division, Royal Infirmary, Glasgow G4 0SF, Scotland **Benzodiazepine drugs in general medical patients.** *British Medical Journal (London).* No. 6011:680-682, 1976.

The use of benzodiazepine derivatives in the medical division of Glasgow Royal Infirmary and a trial to establish their relative potency in insomnia are discussed. A study of the annual records of the Infirmary showed that nitrazepam was used most frequently, with diazepam being second in frequency of use, and phenobarbital, chlorthalidone, amobarbital, and methaqualone being used relatively little. A drug surveillance study of 5288 patients showed 1113 (21%) receiving nitrazepam, usually in a dose of 10mg. Of these 1113 patients, 260 (23%) also received diazepam, and 169 (15%) received another hypnotic or anti-anxiety agent. A total of 836 (16%) patients received diazepam, most receiving doses of 5 to 15mg. Of these 836 patients, 152 received a hypnotic or anti-anxiety agent other than diazepam. In a double-blind study, flurazepam, nitrazepam, diazepam, promethazine, and a placebo were compared in a general medical ward. The patient received one drug on the 3rd night, a second drug on the 4th night, and the two drugs were compared. Patients preferred flurazepam over placebo and promethazine over flurazepam, but there was no significant difference between flurazepam vs. nitrazepam, nitrazepam vs. diazepam, or nitrazepam vs. promethazine. Patients over 65 preferred nitrazepam over promethazine. A few patients reported hangover as a side effect. 9 references.

001834 Kocher, R. Psychiatric and Neurological University Clinic, Basel, Switzerland **The use of psychotropic drugs in the treatment of chronic, severe pains.** *European Neurology (Basel).* 14(6):458-464, 1976.

The results of long experience in the treatment of chronic and severe pains resistant to ordinary therapy with psychotropic drugs are reported. Out of 103 inpatients with chronic and severe pains caused by neurological conditions who were treated with a combination of thymoleptics and neuroleptics, 82 showed marked improvement. These results are

compared with others published in this field. The pharmacological basis of this action, the advantages of the use of psychotropic drugs, especially of the combination of thymoleptics and neuroleptics, is discussed. A dosage schedule for inpatients and outpatients has been established, using imipramine (Tofranil) or chlorimipramine (Anafranil), and haloperidol (Haldol). 19 references. (Author abstract)

001835 Kretschmar, J. H.; Kretschmar, Chr. Psychiatrische Klinik der Universität, Rheinisches Landeskrankenhaus Dusseldorf, Bergische Landstrasse 2, D-4000 Dusseldorf 12, Germany **/Dose effect relationship in treatment with piracetam./ Zur Dosis-Wirkungs-Relation bei der Behandlung mit Piracetam.** *Arzneimittel-Forschung (Aulendorf).* 26(6):1158-1159, 1976.

Piracetam, at a dosage of 800mg t.i.d. and 1600mg t.i.d., was compared with placebo in the treatment of chronic brain syndrome in elderly patients. In the study comparing the lower dose of piracetam with placebo there were 178 patients, 125 women and 53 men, with an average age of 71 years, including 90 patients in the piracetam group and 88 patients in the placebo group. At the end of 6 weeks of treatment no significant difference between the two groups was noted. The higher dose was then compared with placebo in a study comprising 78 patients, 61 women and 17 men, with a mean age of 73 years, including 39 patients in the piracetam group and 39 in the placebo group. The improvement rate after 6 weeks was 69% under piracetam, compared with 31% under placebo. Of the 20 target symptoms, 11 improved under piracetam. 3 references.

001836 Lebedinskiy, M. S.; Bortnik, T. L.; Zel'man, V. L.; Kalandarishvili, A. S.; Ostrovskiy, B. I.; Federmesser, K. I.; Tsetlin, M. G. Moskovskaya gorodskaya psikiatricheskaya bol'nitsa No. 12, Moscow, USSR **/Psychotherapeutic and anesthesiological aspects of nitrous oxide used in the treatment of borderline psychotic states./ O nekotorykh psikhoterapevticheskikh i anesteziologicheskikh aspektakh primeneniya zakisi azota v klinike pogranichnykh sostoyaniy.** *Zhurnal Nevropatologii i psikiatrii imeni S. S. Korsakova (Moskva).* 76(6):916-921, 1976.

Clinical experience with psychotherapy conducted while the patient is under the direct influence, and during the aftereffect period of nitrous oxide/oxygen inhalation is described. The results obtained demonstrate the expediency and efficacy of this type of treatment in a number of patients with borderline states, mainly with depressive, phobic and dyssomnic syndromes. 4 references. (Author abstract modified)

001837 Lingetti, M.; Ciarimboli, M.; Policicchio, D. Ente Ospedaliero Provinciale di Avellino, Divisione Di Geriatria, Avellino, Italy **/Drug therapy in chronic cerebrovascular insufficiency in the elderly./ La terapia delle manifestazioni croniche dell'insufficienza cerebro-vascolare dell'anziano.** *Giornale di Gerontologia (Firenze).* 24(2):82-94, 1976.

A study was made of drug therapy of cerebrovascular insufficiency in 120 patients between 55 and 80 years of age. Simplified versions of the Longmire test and the Robinson test were given to determine the extent of cerebrovascular deficiency and the mental and behavioral status of the patient. Patients were divided into five groups, and were tested at the beginning of the trial, after 15 days and after 25 days. Each group received a different drug. It was concluded that naphthohydrofuryl, vincamine, and pyracetam were effective in reduction of symptoms and that the combination of vincamine with pyracetam produced the best results. 21 references.

001838 Linnoila, M.; Viukari, M.; Hietala, O. Box 2921, Duke University Medical Center, Durham, NC 27710 **Effect of sodium valproate on tardive dyskinesia.** *British Journal of Psychiatry* (London). 129:114-119, 1976.

The effects of sodium valproate, a drug which has been demonstrated to increase gamma-aminobutyric acid levels in the CNS, on tardive dyskinesia and psychiatric symptoms was investigated in a double-blind crossover study on 32 chronic aged psychotic patients. The orofacial dyskinesias were totally or significantly relieved in 17 cases. During the active treatment period, the involuntary movements of the extremities and dystonic spasms were also significantly relieved in 7 out of 9 patients. In two patients, however, the extrapyramidal symptoms became slightly worse. A significant improvement was noted in the psychiatric symptoms of 14 out of 32 patients during sodium valproate administration. The psychiatric state of 4 out of 32 patients deteriorated. There was no correlation between the serum concentration of sodium valproate and its effect on the dyskinesia or on the psychiatric symptoms. Some of the elderly subjects showed a slight accumulation of the drug. 32 references. (Author abstract)

001839 Lomholt, Bjarne Saaby. no address **Treatment of acute poisoning with tricyclic antidepressants by means of hyperventilation. Report of a controlled clinical trial.** *Ugeskrift for Laeger* (Copenhagen). 138:4-9, 1976.

ECG disturbances in acute poisoning with tricyclic antidepressants were treated with prolonged hyperventilation with $pCO_2 = 20$ to 25 mmHg. The investigation comprised 10 patients to whom CO_2 was administered in the inspired air by means of hyperventilation for two periods of 1 hour so that the pCO_2 became normal (41 to 46 mmHg). The heart rate and the width of the QRS complex were measured in the ECG during hypocapnia and normocapnia and the results were analyzed statistically. During hypocapnia, the heart rate was found to be reduced and the QRS complex narrowed. Both of these parameters vary significantly from the conditions present during normocapnia. (Journal abstract)

001840 Loosen, P. T.; Wilson, I. C.; Lara, P. P.; Prange, A. J., Jr.; Pettus, C. Division of Research, North Carolina Department of Mental Health, Raleigh, NC 27611 **Influencing depressive conditions of the alcohol withdrawal syndrome with TRH (thyrotropin releasing hormone).** *Beeinflussung depressiver Zustände im Alkoholentzugssyndrom mit TRH (Thyrotrophin-Releasing-Hormon).* *Arzneimittel-Forschung* (Aulendorf). 26(6):1164-1166, 1976.

The effect of thyrotropin releasing hormone (TRH) on alcohol withdrawal syndrome was studied in 15 alcoholics, 29 to 55 years old, average age 42 years. Only patients who were in a pre-delirious state and had a substantial score on the Hamilton Depression Scale were included. Patients were divided into three groups: 1) receiving 0.5mg TRH in NaCl; 2) receiving 1mg nicotinic acid in NaCl; and 3) receiving NaCl alone. Nicotinic acid was chosen as an active placebo because it simulates certain side-effects of TRH such as flush and feeling of warmth. All injections were i.v. and double-blind. On the day before, and the day of the injection patients were rated on the Hamilton Scale and the Brief Psychiatric Rating Scale (BPRS). TSH and thyroid hormone were assayed. Two patients did not show a normal release of TSH in response to TRH. The day after the injection, a significant remission of depressive symptomatology occurred in all groups. 16 references.

001841 Madsen, J. A.; Bennett, D. R.; Jordan, W. S.; Graves, C. no address **Clinical studies of anesthetic cerebral activation.** *Electroencephalography and Clinical Neurophysiology* (Amsterdam). 41(6):650-651, 1976.

At a meeting of the Western EEG Society in San Antonio in February 1976, a study comparing the effects of ketamine anesthesia and thiopental anesthesia in 20 mentally retarded epileptic patients was described. Ketamine produced dystonia and dyskinesias in 15 of 19 patients. Major support measures for airway maintenance were needed in 63% of the ketamine patients and 15% of the thiopental patients. Ketamine induced major seizures in 9 of 19 patients and minor seizures in one patient; thiopental induced minor seizures in 2 of 20 patients and a major seizure in 1 patient. Patients with poorly controlled seizures and/or multifocal EEG discharges were more likely to have ketamine induced seizures. No such correlation predicted the occurrence of dystonia. It is concluded that thiopental is associated with fewer adverse effects in these patients than is ketamine.

001842 Marini, J. L.; Sheard, M. H.; Bridges, C. I.; Wagner, E., Jr. Department of Psychiatry, Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **An evaluation of the double-blind design in a study comparing lithium carbonate with placebo.** *Acta Psychiatrica Scandinavica* (Copenhagen). 53(5):343-354, 1976.

As part of a study of drug treatment of aggressive behavior to be reported separately, the double-blind procedure was evaluated in a recently completed comparison of the efficacy of lithium carbonate versus placebo in modifying aggressive behavior in nonpsychotic incarcerated delinquents. The side-effects of lithium carbonate were sufficient to reveal the medication to most subjects receiving it. Thus, while the study staff could not identify lithium receivers at better than chance levels, and while subjects who received placebo could not identify their medication at better than chance levels, subjects who received lithium could accurately identify it. On a weekly symptom checklist there was no difference between lithium and placebo groups on average lithium target symptoms reported during 4 week pre- and postmedication control periods; however, lithium receivers reported significantly more target symptoms every week medication was administered. Of 16 subjects who quit the study, 14 had received lithium and nearly all of those who gave reasons for quitting specified side-effects, most often nausea. The methodological problems of using lithium in a double-blind design might be overcome by employing a discontinuation design, or, speculatively, a double-blind, cross over design utilizing an active placebo. 13 references. (Author abstract)

001843 McFarlain, Robert A.; Mielke, David H.; Gallant, Donald M. Department of Psychiatry, Tulane University School of Medicine, New Orleans, LA 70112 **Comparison of muscle relaxation with placebo medication for anxiety reduction in alcoholic inpatients.** *Current Therapeutic Research*. 20(2):173-176, 1976.

The effectiveness of group muscle relaxation administered via taped instructions was compared to that of placebo medication for reduction of anxiety of chronic alcoholics in a residential treatment program after withdrawal. No superiority of relaxation training over placebo medication was shown in this study. This fact is not too surprising because two of the better antianxiety agents available (clorazepate dipotassium and diazepam) were also not clearly superior to placebo in the drug efficacy study from which the placebo data were drawn. Anxiety reduction resulting from the extensive therapy availa-

ble to the patients in the carefully planned ward milieu undoubtedly masks additional therapeutic gains from chemotherapy or behavior therapy. 7 references. (Author abstract)

001844 McNeil, H. Graham, Jr.; Rogers, Michael V.; Matthews, Hewitt W. Department of Pharmaceutical Chemistry, Mercer University, Southern School of Pharmacy, Atlanta, GA **Drug therapy in the hyperkinetic syndrome.** *Urban Health.* 5(4):12-14, 1976.

Diagnosis, etiology and drug of treatment of hyperkinesis (minimal brain dysfunction) are briefly discussed. The treatment of choice is seen to be drug therapy. Evaluations of the following drugs are given: psychostimulants, dextroamphetamine, methylphenidate, levoamphetamine, pemoline, neuroleptic agents, deanol, minor tranquilizers, tricyclic antidepressants, and lithium carbonates. Special diets and thyrotropin releasing hormone are also briefly discussed. 17 references.

001845 Mindus, P.; Cronholm, B.; Levander, S. E.; Schalling, D. Department of Psychiatry, Karolinska Institute, S-104 01 Stockholm 60, Sweden **Piracetam-induced improvement of mental performance: a controlled study on normally aging individuals.** *Acta Psychiatrica Scandinavica* (Kobenhavn). 54(2):150-160, 1976.

A double-blind, intraindividual, crossover comparison of the mental performance of 18 aging, nondeteriorated individuals during two four week periods of piracetam (1-acetamide-2-pyrrolidone) and placebo administration was performed using conventional and computerized perceptual motor tasks. In a majority of these tasks the subjects did significantly better when on piracetam than on placebo, a finding consistent with ratings completed by two independent observers. The findings indicate new avenues for the treatment of individuals with reduced mental performance possibly related to disturbed alertness (a neglected group of psychiatric conditions). 30 references. (Author abstract)

001846 Montanari, C.; Vallecorsi, G. F. no address **Clinical trial with amantadine and pemoline in paralysis agitans.** *Age and Ageing* (London). 5:6-11, 1976.

Amantadine and pemoline were compared in elderly patients with parkinsonism. Patients' subjective symptoms and clinical opinions of physicians and auxiliary medical personnel were evaluated. Amantadine in a dose of 400mg/day was found to be superior to placebo, but led to side-effects. At a dose of 200mg/day, therapeutic efficacy was null or doubtful. Combination amantadine with pemoline led to clinical remission with a small percentage of side effects. 24 references.

001847 Nash, Ralph J. Medical Research Department, Hoechst-Roussel Pharmaceuticals, Inc., Somerville, NJ **Clinical research on psychotropic drugs and hyperactivity in children.** *School Psychology Digest.* (4):22-33, 1976.

A review of the various stages of research and clinical testing of psychopharmacologic drugs together with an overview of the use of various classes of drugs and evaluation of drug medication response in hyperactive children are presented. Included are a discussion of various clinical testing methods and rating scales and a discussion of various groups of psychotropic tranquilizers, antidepressants, anticonvulsants, psychostimulants and lithium. 43 references.

001848 no author. no address **The drug treatment of parkinsonism.** *New Zealand Medical Journal* (Dunedin). 84(568):67-68, 1976.

The drug treatment of parkinsonism is reviewed. Levodopa is the most effective treatment to date, with 4/5 of patients improving on a dose of 2g/day. Side effects are nausea and vomiting, involuntary movements, delirium, hypomania, and postural hypotension. Since levodopa is effective for up to 4 hrs only, akinesia may occur when the effect of the drug wears off. At the peak plasma level, which occurs about 2 hrs after administration, episodes of dyskinesia may occur. Wild swings from gross parkinsonism to considerable activity may occur several times a day in patients on chronic levodopa therapy; this is the on/off effect and is nearly impossible to treat. Addition of carbidopa, a decarboxylase inhibitor, allows use of a smaller dose of levodopa and is associated with a decreased incidence of nausea and vomiting, but does not improve the clinical effectiveness of levodopa. Anticholinergic drugs and amantadine should be used only if levodopa fails. Dopamine agonists under study include piribedil, apomorphine, bromocriptine, and ergotriple. All cause nausea, dyskinesia, mental disturbance, and drowsiness. When the tremor does not respond to treatment, propranolol or stereotactic surgery may be helpful. 4 references.

001849 no author. no address **Beta-adrenergic blockade and anxiety.** *Lancet* (London). No. 7986:611-612, 1976.

The use of beta-adrenergic blocking agents in the treatment of anxiety is discussed. These drugs are effective only in somatic anxiety or when inappropriate sympathetic activity contributes to the anxiety. The beta-adrenergic blocking agents probably act peripherally rather than centrally. They are helpful in anxiety induced tremor, functional heart conditions induced by anxiety (increased cardiac output, supraventricular tachycardia, labile hypertension), palpitations, trembling, giddiness, dizziness, shaking, and blushing. Patients with primarily psychic anxiety are not helped much by beta-blockers. It is best to start patients on 10 to 20mg propranolol t.i.d. or q.i.d., although the dose may have to be increased for the best therapeutic response. These drugs have few side-effects, and there is little chance of drowsiness, tolerance, dependence, or abuse. 16 references.

001850 Palestine, Milton L.; Alatorre, Ernest. no address **Control of acute alcoholic withdrawal symptoms: a comparative study of haloperidol and chlordiazepoxide.** *Current Therapeutic Research.* 20(3):289-299, 1976.

The effectiveness of haloperidol in controlling acute alcoholic withdrawal symptoms was compared with that of chlordiazepoxide in a double-blind study. Symptoms were successfully controlled within the 4 hr study period in 70% of the patients treated with haloperidol and in 44% of the patients treated with chlordiazepoxide. Greater reduction in severity of target symptoms and brief psychiatric rating scale (BPRS) symptoms were achieved with haloperidol. There were no significant adverse reactions and no alterations in laboratory results of hematologic tests, hepatic tests or renal tests occurred with either drug. It is suggested that haloperidol may be the drug of choice in treating symptoms of acute alcohol withdrawal. 11 references.

001851 Petrich, C.; Voss, H. v.; Bretschneider, A.; Gobel, U. Universitäts-Kinderklinik II, Moorenstr. 5, D-4000 Düsseldorf, Germany **/Heroin withdrawal syndrome in newborns./** *Heroin Entzugssyndrom beim Neugeborenen.* *Klinische Pädiatrie* (Stuttgart). 188(6):552-553, 1976.

A case of severe heroin withdrawal in a newborn infant is reported. Incidence of this phenomenon seems to be increasing in West Germany. The clinical symptoms of tremor, vomiting, crying, rapid breathing, fever, and convulsions are listed; a general therapy of chlorpromazine and phenobarbital is recommended. 10 references.

001852 Rappolt, Richard T.; Gay, George; Inaba, D. S.; Rappolt, Nancy R. Clinical Toxicology, Suite 403, 4141 Geary Boulevard, San Francisco, CA 94118 **Propranolol in cocaine toxicity**. *Lancet* (London). No. 7986:640-641, 1976.

In a letter to the editor of *Lancet*, the use of propranolol to reverse the cardiovascular pressor effects of cocaine is reported. The patient with chronic cocaine toxicity is a prime candidate for cerebrovascular accident, cardiac arrhythmia, or congestive heart failure. A case report is given of a 28-year-old male who had ingested cocaine along with alcohol and other drugs and presented with tachycardia and hyperpnea. He was successfully treated with 2mg propranolol.

001853 Resnick, Richard B.; Orlin, Lois; Geyer, Gretchen; Schuyten-Resnick, Elaine; Kestenbaum, Richard S.; Freedman, Alfred M. Division of Drug Abuse Research and Treatment, New York Medical College, 5 E. 102nd St., New York, NY 10023 **1-alpha-Acetylmethadol (LAAM): prognostic considerations**. *American Journal of Psychiatry*. 133(7):814-819, 1975.

The responses of 28 adult male volunteers who were openly changed from methadone to 1-alpha-acetylmethadol (LAAM) maintenance were studied. It was found that patients who had been receiving middle range doses (50 to 70mg) of methadone required a significantly lower mean increase in LAAM than patients who had been receiving either high or low methadone doses and that the patients who accepted LAAM differed significantly from those who did not in MMPI 2 point code ratings and mean psychosocial adjustment scale scores. These findings may provide prognostic indicators for response LAAM, a possible alternative to methadone. 26 references. (Author abstract)

001854 Ross, Dorothea M.; Ross, Sheila A. no address **Hyperactivity: research, theory, and action**. New York, Halsted Press, 1976. 380 p. \$18.95.

Current knowledge about hyperactivity is surveyed, with emphasis on behavioral, rather than medical aspects. Clinical and empirical evidence that hyperactivity exists from infancy through adulthood is presented. Topics discussed include: the hyperactive child's own view of the problem, strategies for prevention, and the possible etiological connection of some environmental factors. Drug therapy, psychotherapy, and behavior therapy are described and evaluated. Treatments which may be partially implemented by parents and other non-professionals are also discussed.

001855 Safer, Daniel; Allen, Richard. no address **Hyperactive children**. Baltimore, University Park Press, 1976. 239 p. \$8.50

A text on practical methods to help professionals successfully manage hyperactive children is presented. It includes chapters on such diverse topics as the pharmacological management of hyperactivity; clinical forms and evaluation tests; behavior management in the classroom and home; and educational management. Individual topics covered include the use, dosage, clinical trials and side effects of psychostimulants; various forms of evaluative testing and questionnaires; practical and workable suggestions for counseling parents; and

appropriate use of positive and negative reinforcement contingencies. Also presented is a comprehensive plan of behavioral management based on a coordinated multimodal approach. Drugs discussed are Dexedrine, Ritalin and Cylert, including dose and dose schedule, drug trial and side effects.

001856 Savage, Charles; Karp, Elaine G.; Curran, Stephen F.; Hanlon, Thomas E.; McCabe, O. Lee. Department of Psychiatry, VA Hospital, Baltimore, MD 21218 **Methadone/LAAM maintenance: a comparison study**. *Comprehensive Psychiatry*. 17(3):415-424, 1976.

Effects and success of methadone and 1-alpha-acetylmethadol (LAAM) treatment of 99 heroin addicted patients are compared. Data on demographic variables, EEG results, blood chemistry and hematology measures, and personality measures were examined. LAAM is a longer acting methadone derivative requiring only three doses per week instead of daily doses of methadone. Lower acceptance and higher dropout rates with LAAM therapy indicated patient unfamiliarity and apprehension with the drug; lack of a methadone rush within 2 hours of dosing; increased complaints of side-effects after switching medications. Relative safety of both drugs was shown to be similar. Although personality assessments for those receiving each drug were similar, it was noted that there were definite differences in psychological measurement of those in the program who became dropouts. 5 references.

001857 Schou, Mogens; (Dufour, H., Translator). Statshospitalet, DK-8240 Risskov, Denmark **Indications for lithium salt in other than manic-depressive psychosis**. *Indications des sels de lithium en dehors de la psychose maniaco-depressive*. *Evolution Psychiatrique* (Toulouse). 41(3):533-549, 1976.

Deomonstrated proposed and refuted indications for use of lithium in psychiatric diseases other than manic depression and nonpsychiatric diseases are discussed. Administration of lithium is proposed in: mania and hypomania, depression, schizophrenia, bipolar recurring affective psychoses, monopolar recurring affective psychoses, recurring schizoaffective psychoses, pathological emotional instability in children and adolescents, periodic pathological aggression, periodic alcoholism with depression, drug addiction, obsessive neurosis, anxiety crisis, and premature dysphoria. The possible use of lithium is discussed in some detail in: emotional instability, hyperkinetic syndrome, periodic pathological aggression, obsession, psychosomatic disorders, dyskinesia, and Meniere's vertigo. 106 references.

001858 Segal, R.; Everson, A.; Sellers, E. M.; Thakur, R. Narcotic Dependence Program, Addiction Research Foundation, 33 Russell St., Toronto, Ontario M5S 2S1, Canada **Failure of acetylmethadol in treatment of narcotic addicts due to nonpharmacologic factors**. *Canadian Medical Association Journal* (Ottawa). 115(10):1014-1016, 1976.

Seventeen subjects, former heroin users currently under methadone treatment, entered a study to determine the toxicity and efficacy of acetylmethadol, a new narcotic substitute with a longer duration of action than methadone. Only nine of the subjects completed the assessment phase of the study and entered the acetylmethadol phase, and only one completed the entire eight week study. The high attrition rate was found to be unrelated to pharmacologic factors; rather, the subjects were concerned that if acetylmethadol proved to be effective, there would be no more methadone to take home and hence no opportunity to trade, sell, or experiment with it. The difficulty in assessing the efficacy of specific drug treatments for

addicted patients thus is underscored. 18 references. (Author abstract modified)

001859 Sewell, Janet; Werry, J. S. School of Medicine, University of Auckland, Auckland, New Zealand **Some studies in an institution for the mentally retarded.** *New Zealand Medical Journal* (Dunedin). 84(574):317-319, 1976.

Patient characteristics and psychotropic drug use were studied in a New Zealand hospital for the mentally retarded. The majority of patients appeared permanent, 80% having been there 5 years. Ages ranged from 2 to 71 years and the majority of patients were mildly or moderately retarded. Patients were separated by sex and the majority lived on large wards of approximately 50 with appropriate nursing staffs. A recent development of allowing male and female patients to live in a more nearly normal living situation was still in the trial stage. Most patients previously had lived within 2 hours driving time of the hospital. Visiting was proportional to time in hospital, degree of retardation and distance of home from hospital. Forty percent of the patients were on psychotropic medication for behavioral control, with long acting drugs given several times a day. Average time on present medication was 1 year. A subgroup of patients taken off medication deteriorated behaviorally according to staff observations. 2 references. (Author abstract modified)

001860 Shetty, Taranath; Chase, Thomas N. Section of Reproduction and Developmental Medicine, Brown University, 50 Maude St., Providence, RI 02908 **Central monoamines and hyperkinesis of childhood.** *Neurology*. 26(10):1000-1002, 1976.

To determine whether hyperkinetic children have abnormalities in resting levels or amphetamine induced alterations in the principal metabolites of dopamine and serotonin in lumbar spinal fluid, 23 hyperkinetic children and 6 normal controls were observed with and without amphetamine pretreatment. Results indicate that lumbar cerebrospinal fluid levels of homovanillic acid and 5-hydroxyindoleacetic acid, the major metabolites of dopamine and serotonin, respectively, in hyperactive children did not differ significantly from those of age matched controls. Dextroamphetamine treatment substantially reduced the spinal fluid content of homovanillic acid but not of 5-hydroxyindoleacetic acid. No change in levels of either monoamine metabolite occurred with placebo therapy. In hyperactive children receiving dextroamphetamine, the amount of homovanillic acid decline correlated closely with the degree of clinical improvement. These results support the view that an alteration in central dopamine mediated synaptic function may occur in children manifesting the hyperactive syndrome. 20 references. (Author abstract modified)

001861 Simonsen, N.; Olsen, P. Zander, Kuhl, V.; Lund, M.; Wendelboe, J. Department of Neurology, Glostrup Hospital, Glostrup, Denmark **A comparative controlled study between carbamazepine and diphenylhydantoin in psychomotor epilepsy.** *Epilepsia* (Amsterdam). 17(2):169-176, 1976.

A double-blind study of the antiepileptic effect and side effects of carbamazepine (CARB) and diphenylhydantoin (DPH) was undertaken in 38 patients with psychomotor epilepsy and without grand mal epilepsy except for a single previous seizure. The patients were treated with CARB and DPH only, each in periods of 16 weeks and with a crossover of 4 weeks. The initial dosage of 6mg/kg DPH or 15mg/kg CARB was corrected according to the serum values aiming at therapeutic intervals of 8-16mg/l DPH and 6-10mg/l CARB. The trial had to be discontinued in 12 patients. The effect of the two drugs in

preventing psychomotor seizures was the same. Some patients, however, had considerably fewer seizures while on CARB; others had fewer seizures on DPH. It seems advisable, therefore, to try both drugs separately before proceeding to combined medication. During CARB treatment the selected therapeutic interval was more easily reached and maintained than during DPH. During the latter treatment, one third of the monthly serum value determinations were below the level in spite of dosage corrections. Side effects were equally mild and occurred as often during DPH as during CARB treatment. 13 references. (Author abstract)

001862 Stanski, Donald R.; Greenblatt, David J.; Selwyn, Adrian; Shader, Richard I.; Franke, Kate; Koch-Weser, Jan. Department of Anesthesia, Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Plasma and cerebrospinal fluid concentrations of chlorthalidone and its metabolites in surgical patients.** *Clinical Pharmacology and Therapeutics*. 20(5):571-578, 1976.

Concentrations of chlorthalidone (CDX) and its metabolites in plasma and cerebrospinal fluid (CSF) of a series of patients receiving spinal anesthesia for surgical procedures were determined in a study of the pharmacokinetics of anti-anxiety drugs in the central nervous system. Thirty otherwise healthy patients received a 100mg oral dose of CDX hydrochloride just prior to surgical procedures, 14 of them having also received 100mg on the night before surgery. Simultaneous samples of venous blood and CSF were taken immediately prior to injection of spinal anesthesia and were assayed for concentrations of CDX and its major metabolite, desmethylchlorthalidone. Plasma concentrations of CDX were higher than simultaneous CSF concentrations. Equilibration of CDX between plasma and the lumbar sampling site appeared to be complete within two hours of the most recent dose. After attainment of distribution equilibrium, simultaneous plasma and CSF concentrations of CDX were highly correlated, with a mean CSF/plasma concentration ratio of only 0.043. The limited passage of CDX into human CSF is suggested as probably due to extensive binding to plasma protein. Assuming that transfer of CDX from plasma to CSF is governed by passive diffusion, the extent of plasma protein binding of CDX in healthy individuals averages about 96%. 22 references. (Author abstract modified)

001863 Steinhausen, H.-Ch. Universitäts-Kinderklinik, Martinstr. 52, D-2000 Hamburg 20, Germany **/Hyperkinetic syndrome./ Das hyperkinetische Syndrom.** *Klinische Pädiatrie* (Stuttgart). 188(5):396-407, 1976.

Hyperkinetic syndrome is reviewed, including symptoms, prevalence, etiopathogenesis, therapy and theory. Of the three types of therapy (psychotherapy, drug therapy, and special education), drug therapy is especially emphasized. Results obtained in the use of methylphenidate, dextroamphetamine, imipramine, lithium carbonate, chlorpromazine, thioridazine, haloperidol, chlorthalidone, and caffeine are discussed. Zentall's theory of optimal stimulation is presented as a most cogent explanation of the hyperkinetic syndrome. 78 references.

001864 Totman, Richard. Nuffield College, Oxford, England **Cognitive dissonance in the placebo treatment of insomnia -- a pilot experiment.** *British Journal of Medical Psychology* (London). 49(Part 4):393-400, 1976.

The application of cognitive dissonance theory was attempted in the placebo treatment of insomnia in 11 hospital patients. It was found that patients who were required to make

meaningful decisions concerning their treatment derived significantly greater hypnotic therapeutic value from placebo therapy than patients whose treatment was simply administered to them. It is suggested that post decisional dissonance may be a successful therapeutic agent in treatment of insomnia. 8 references.

001865 Tuma, A. Hussain; Kline, Nathan S.; Razani, Javad; Wahabzadeh, Azim. Clinical Research Branch, DERP, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20014 **A controlled study of the treatment of narcotic addiction in Iran: a preliminary report (Unpublished paper)**. NIMH, Rockville, MD 1976. 33 p.

A research plan followed in evaluating the efficacy of two pharmacological approaches (methadone maintenance and combination antidepressant/tranquilizer therapy) used in the treatment of drug abuse in a program conducted in Iran is presented and discussed. It is reported that: 1) the therapeutic interventions used (drug treatment, psychotherapy, social case work) prevented relapse in about 70% of the patients over a 9 month period; 2) in general, patients who maintained their medication and contact with the staff tended to abstain from narcotic drugs or to use them only occasionally, while those who discontinued their treatment tended to relapse to regular use of narcotics; and 3) the level of postwithdrawal depression could be correlated with the use of illicit narcotic drugs, rehospitalization for addiction, employment status and income. The fact that these are preliminary findings obtained with a relatively small number of patients is stressed.

001866 Whalen, Carol K.; Henker, Barbara. Program in Social Ecology, University of California, Irvine, CA 92717 **Psychostimulants and children: a review and analysis**. Psychological Bulletin. 83(6):1113-1130, 1976.

Results of psychostimulant medication for children are reviewed in three areas; motor activity, attention and cognition, and social/adaptive behavior. Prevailing misconceptions about these drugs and the children who take them are examined, as are the disparities between findings on short-term and long-term effects. The dearth of knowledge and theory regarding psychological concomitants of stimulant medication is noted, and a sociocognitive analysis of drug effects is proposed. Recent research on causal attributions is reviewed, and a set of hypotheses and research strategies is developed, centering on the proposition that stimulant medication is a powerful source attributional change in both the child and others. A major conclusion is that predicting and enhancing medication effects may depend on understanding and modifying the social and cognitive sequelae of drug intervention. A further suggestion is that the prevalence and import of psychoactive drug use make this a fruitful area for testing attribution and expectancy theories. 113 references. (Author abstract)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

001867 Dittrich, A.; Bickel, P.; Schopf, J.; Zimmer, D. Psychiatrische Universitätsklinik Burgholzli, Forschungsdirektion, Postfach 68, CH-8029 Zurich, Switzerland **Comparison of altered states of consciousness induced by the hallucinogens (-)-delta9-trans-tetrahydrocannabinol and N,N-dimethyltryptamine./ Vergleich veränderter Bewusstseinszustände unter den Halluzinogenen (-)-delta9-trans-Tetrahydrocannabinol (delta9-THC) und N,N-Dimethyltryptamin (DMT)**. Archiv für Psychiatrie und Nervenkrankheiten (Berlin). 223(1):77-87, 1976.

Altered states of consciousness induced by the hallucinogens (-)-delta9-trans-tetrahydrocannabinol (delta9-THC) and N,N-dimethyltryptamine (DMT) were compared using two placebo control groups. A total of 24 subjects received THC and 26 subjects were treated with DMT. Placebo was given to 24 subjects. The effects were assessed by a questionnaire administered following the experimental conditions. Questionnaire items were combined into the following eight scales according to their content and several criteria of the theory of mental testing: visual hallucinations (illusions), auditory hallucinations (illusions), impairment of memory and attention, depersonalization syndrome, derealization syndrome, changes of body image, euphoric state and anxious/depressive state. The two hallucinogen groups differed significantly from placebo on all eight scales. No difference, however, between THC and DMT was significant. On the scale "optical hallucinations (illusions)," a tendency that DMT might have stronger effects than THC was found. Methodological problems of comparing different hallucinogens are discussed. 27 references. (Journal abstract modified)

001868 Hunt, Harry T.; Chefurka, Cara M. Department of Psychology, Brock University, St. Catharines, Ontario L2S 3A1, Canada **A test of the psychedelic model of altered states of consciousness: the role of introspective sensitization in eliciting unusual subjective reports**. Archives of General Psychiatry. 33(7):867-876, 1976.

An examination is made of the term psychedelic as applied to altered states of consciousness. Such subjective anomalies are suggested to be direct expressions of normal psychological functioning. It is felt that the anomaly in such experience would depend in the first instance on sensitization to qualities of immediate subjective state. Such sensitization should in itself be considered nonadaptive, cutting off the "intentionality" of psychic functioning at a microgenetically primitive level. This hypothesis was tested among 44 and 48 student subjects in 2 consecutive years respectively in a setting involving isolation and inactivity for a period of 10 minutes. The incidence of anomalous subjective reports in groups provided instructions involving direct sensitization to immediate subjective state was compared with nonsensitization groups. In addition, as anticipated from a "psychedelic" model of altered states, a study of the experimental protocols of the early introspectionists revealed subjective anomalies similar to those found in drug and meditative states. 58 references. (Author abstract modified)

001869 Koukkou, M.; Lehmann, D.; Zimmer, D.; Wyss, U. no address **Tendency to cannabis-induced hallucinations indicated by predrug EEG**. Electroencephalography and Clinical Neurophysiology (Amsterdam). 41(6):665, 1976.

At a meeting of the German EEG Society in Munster in 1975, research on the variability in subject response to oral administration of delta9-tetrahydrocannabinol (THC) caused by differing responsiveness of the CNS and the EEG indicators of differing responsiveness was described. Subjects were divided into high hallucinators and low hallucinators, based on postdrug self-rating reports. The average spectra of the low hallucinators were different from those of the high hallucinators, both before and after THC ingestion. Low hallucinators had slower alpha peak frequency, slower alpha activity and faster theta activity than high hallucinators. Spectra of high hallucinators resembled those of subjects with high neuroticism scores and did not resemble spectra of schizophrenics.

001870 Naylor G. Department of Psychiatry, University of Dundee, Dundee DD1 4HN, Scotland **Prediction of clinical response to lithium.** *Lancet* (London). 2(7988):749-750, 1976.

Results of studies of the ratio of lithium concentration in erythrocytes and plasma were examined in an attempt to predict clinical response to lithium. The mesolimbic dopaminergic system, rather than the nigrostriatal tract, is considered as the site of action of antipsychotic drugs. The effects of neuroleptics, antiepileptics, cholinomimetics, and morphine on the levels of two dopamine metabolites, in the neostriatum and two limbic structures of the rat brain were investigated. It is concluded that neuroleptics with a low frequency of extrapyramidal side-effects are differentiated from the classical neuroleptics by their ability to produce a relatively large increase in DOPAC and H.V.A. levels in the two limbic regions. Although patients who do well on lithium may differ on some biochemical parameter from those who do poorly on lithium, the design must carry a proper control in order to establish that the difference is due to the lithium and is not simply a feature of the natural history of the illness. It was found that the erythrocyte plasma lithium ratio is not stable since it changes with change in plasma concentration. Even the mechanism underlying the distribution of lithium is not clear. The results from studies of the ratio of lithium concentration in erythrocytes and plasma must, therefore, be interpreted with considerable caution. 7 references. (Author abstract modified)

001871 no author. no address /**Induced psychosis from ingestion of *Datura suaveolens*.** Angel's trumpet may herald psychosis. *Medical World News*. 17(18):19, 1976.

Diagnosis of the effects of the ingestion of angel's trumpet (*Datura suaveolens*) are reported in cases recorded in Brevard County, Florida as a means for identification of the psychedelic response and possible liver damage. The plant contains several solanaceous alkaloids, particularly atropine, hyoscyamine, and hyoscyne (scopolamine). Physical effects recorded include: high temperature, high pulse, wide blood pressure ranges, dilated pupils, extreme hyperactivity, and diminished muscular strength. Three beat clonus and Babinski's signs were reported. Patients were observed to be confused, agitated, belligerent and delirious, and visual hallucinations were reported. Treatment consisted of the administration of IV physostigmine salicylate with a suggested sedative of benzodiazepine.

001872 Noyes, Russell, Jr.; Brunk, S. Fred; Avery, David H.; Canter, Arthur. Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Psychologic effects of oral delta9-tetrahydrocannabinol in advanced cancer patients.** *Comprehensive Psychiatry*. 17(5):641-646, 1976.

Delta9-tetrahydrocannabinol (THC), the active ingredient in marihuana, was given as an experimental analgesic to 46 patients with cancer pain in a controlled hospital environment in order to compare the analgesic properties with codeine. THC demonstrated sedative effects in contrast to the stimulating ones commonly associated with its social use. It is concluded that THC is a mild analgesic in patients with cancer pain and produces relaxation, mild mood elevation, appetite stimulation, and a degree of analgesia, effects which could prove useful in cancer patients. Identification of the side-effects of THC in a treatment setting and establishment of the limits of its safety are required. 14 references.

001873 Peeke, Shirley C.; Jones, Reese T.; Stone, George C. Langley Porter Neuropsychiatric Institute, University of

California, San Francisco Medical Center, San Francisco, CA 94143 **Effects of practice on marihuana-induced changes in reaction time.** *Psychopharmacology* (Berlin). 48(2):159-163, 1976.

The effect of smoked marihuana on performance of complex reaction time (RT) tasks was studied in two groups of subjects. Significant RT slowing was found in the first testing session in subjects performing during marihuana intoxication without prior practice. Performance of these subjects improved rapidly; by the end of the second testing session performance was not different from undrugged performance. Subjects receiving practice before performance under marihuana intoxication showed no marihuana induced RT slowing. It is suggested that reaction time performance may involve two phases: an early, attention demanding phase which is sensitive to drug effects, and a later phase which results from practice and is more resistant to drug effects. It was also determined that 4 days of repeated marihuana usage produces only slight reductions in pulse rate, salivary flow and subjective responding. 13 references. (Author abstract modified)

001874 Rouger, E. 118, boulevard Diderot, Pairs, F-75012 France /**Indications for sultopride, a major neuroleptic.** Les indications du sultopride, neuroleptique majeur. *Psychologie Medicale* (Paris). 8(6):939-942, 1976.

The indications and side effects of sultopride, an anisamide derivative, are discussed. The indications are: manic agitation, delirious outbursts, agitation and psychomotor excitation, acute schizophrenia, character and behavior problems, chronic alcoholism, alcoholic confusion, impulsiveness and aggressiveness in epileptics, mental retardation, senility, chronic psychotic delirium, paranoia, and chronic hallucinatory psychoses. Side effects are extrapyramidal symptoms, anticholinergic symptoms, anxiety, depersonalization, somnolence, and rare endocrine symptoms (amenorrhea, galactorrhea). The dosage is 1 to 1.6g/day i.m. or 2 to 3g/day orally. 13 references.

001875 Saidel, Donald R.; Babineau, Raymond. Womack Army Hospital, Fort Bragg, NC **Prolonged LSD flashbacks as conversion reactions.** *Journal of Nervous and Mental Disease*. 163(5):352-355, 1976.

Prolonged LSD flashbacks are discussed as conversion reactions in a case study of the background and psychotherapeutic treatment of a patient with prolonged LSD flashbacks. The hypothesis that flashbacks can be psychologically determined symptoms is supported by the dynamics of the case and the course of treatment. A second focus is a partial explanation for the frequent observation that obsessive-compulsive personalities are at increased risk for LSD flashbacks. 7 references. (Author abstract)

001876 Shopsin, Baron; Kline, Nathan S. Neuropsychopharmacology Research Unit, New York University Medical Center, New York, NY **Monoamine oxidase inhibitors: potential for drug abuse.** *Biological Psychiatry*. 11(4):451-456, 1976.

It is suggested that both amphetamines and monamine oxidase (MAO) inhibitors share common clinical and pharmacological properties which make them susceptible to becoming drugs of abuse. Both classes of drugs clinically induce euphoriant/stimulating and psychotomimetic effects in certain individuals, and increase, by different mechanisms, the amount of functionally available catecholamines and indoleamines at the receptor site in the brain. It is contended that the clinical association between MAO inhibitor use and dependence and/or tolerance is well established, and an illus-

trative case history of a 52-year-old man who abused such a drug in the course of his psychiatric treatment is presented. It is suggested that such clinical findings of MAO inhibitor dependence will converge with other clinical and biochemical data in helping to define the specific amines responsible for both clinical effects and etiopathogenesis of major psychiatric illnesses such as affective disorders and schizophrenia. 28 references (Author abstract modified)

001877 Yensen, Richard; DiLeo, Francesco; Rhead, John C.; Richards, William A.; Soskin, Robert A.; Turek, Brahim; Kurland, Albert A. Clinical Sciences Division, Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228
MDA-assisted psychotherapy with neurotic outpatients: a pilot study. *Journal of Nervous and Mental Disease.* 163(4):233-245, 1976.

Ten neurotic patients (five males and five females) were treated over a period of 2 to 6 months as outpatients. The study allowed for a maximum of 75 hours of psychotherapy. During the course of treatment, two to four administrations of methylenedioxymphetamine (MDA) were employed as adjunctive aids in an effort to enhance the psychotherapeutic process. The mean duration of the drug sessions was 8 hours. The first administration of MDA took place when, in the therapist's judgment, sufficient rapport had been established with the patient. All patients received an initial dose of 75mg of MDA; subsequent dosage was allowed to range up to 200mg. The drug appeared to be well tolerated with no serious side effects or complications observed. Psychometric assessments were obtained pretreatment and posttreatment, employing the Minnesota Multiphasic Personality Inventory (MMPI), Wittenborn Psychiatric Rating Scales (WPRS), Brief Psychiatric Rating Scale (BPRS) and a Social History Questionnaire (SHQ). Followup evaluations were obtained 6 months after the termination of therapy by the use of the MMPI, WPRS, BPRS, and a Social History Questionnaire which had also been administered before treatment was initiated. Clinically, the impression was obtained that psychotherapy and the adjunctive use of MDA appeared to facilitate improvement in these patients. This impression was substantiated by significant reductions in scores on the psychometric assessments measuring depression, anxiety, and obsessive-compulsive traits. The measures evaluating the sense of well-being and self-actualization also were encouraging. Although some of the patients were not as responsive as others, there were no observations to suggest that the condition of any of these patients had become worse. 26 references. (Author abstract)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

001878 Ackenheil, M.; Brau, H.; Burkhart, A.; Franke, A.; Pacha, W. Psychiatrische Klinik, Universität München, Nussbaumstrasse 7, D-8000 München 2, Germany / **Antipsychotic effectiveness in relation to plasma level of clozapine.** *Antipsychotische Wirksamkeit im Verhältnis zum Plasmaspiegel von Clozapin.* *Arzneimittel-Forschung (Aulendorf).* 26(6):1156-1158, 1976.

An attempt was made to correlate the plasma level of clozapine with its therapeutic effect and its side-effects. A group of 26 hospitalized patients, 119 males and 7 females, 16 to 57 years old, mean age 34 years, was studied. Clozapine dosage ranged from 100mg/day to 600mg/day. Plasma concentration of clozapine were determined either by gas chromatography or radioimmunoassay. A significant linear correlation was

found between dosage per body weight and plasma concentration of clozapine. All patients improved. There was no connection between degree of improvement and plasma level of clozapine. All patients showed tiredness and a tendency to fall asleep during the day. These symptoms reached a maximum on the 3rd day of treatment and then declined. Orthostatic dysregulation was most severe on the 2nd day of treatment and then declined with continued treatment. There was no relationship between plasma level of clozapine and these side-effects. 11 references.

001879 Albrecht, J.; Müller-Oerlinghausen, B. Psychiatrische Klinik, Freie Universität Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany / **Clinical significance of intraerythrocyte lithium concentration: results of a catamnestic study.** *Zur klinischen Bedeutung der intraerythrozytären Lithiumkonzentration: Ergebnisse einer katamnesticischen Studie.* *Arzneimittel-Forschung (Aulendorf).* 26(6):1145-1147, 1976.

Because lithium ion concentrations in the rat showed a parallel concentration in the brain and in red blood cells, lithium concentration in red blood cells of patients under lithium therapy was determined. Subjects were 34 patients, 29 female and 5 male, 26 to 68 years of age, who had received lithium therapy for at least 3 years. Lithium and potassium ion concentrations were determined an average of 9 times per patient during a period of 15 months. The average erythrocyte lithium concentration was 0.249mM and the average plasma lithium concentration was 0.735mM, giving an intra/extracellular quotient of 34%. Intraindividual variability of erythrocyte lithium concentrations was 5 to 53%, and the intra/extracellular quotient varied from 8% to 45%. Corresponding values for potassium ion varied by only a factor of 3. Patients under 50 years of age had the same concentrations as the older patients, but required a 50% higher dose of lithium. Side-effects such as tremor or thirst correlated well with intraerythrocyte lithium level, and somewhat less well with plasma lithium level. No connection was found between intra/extracellular lithium quotient and diagnosis or therapeutic response. 8 references.

001880 Antal, J.; Dome, L. First Department of Neurology and Psychiatry, Semmelweis University Medical School, Budapest, Hungary / **Reaction time of normal individuals to long-term Trioxazine.** *Therapia Hungarica (Budapest).* 24(1):10-14, 1976.

The effect of three tablets of Trioxazine for 1 and 2 weeks respectively on visuomotor reaction time is studied in 18 healthy, young medical students in the period preceding their exams. It was found that reaction time improved on Trioxazine slightly but significantly, compared to cases on placebo or no medication. This effect was also noticeable when flashed light fell not on the macula but on the peripheral area of the retina. Trioxazine furthermore overcame the adverse effect of monotonous sound delaying reaction time. Placebo failed to elicit the above described effects of Trioxazine; the values of individuals on placebo corresponded to those of untreated individuals and to normal values. After studies concerned with the role of hemispherical dominance from the viewpoint of occipital afferentation the former was found to be less marked than in connection with the parietal or the frontal lobe. It also became evident that reaction time was affected more markedly by loud monotonous sounds belonging to the domains of infrasound and normal sounds than by ultrasound. 11 references. (Author abstract)

001881 Axelrod, Julius. Laboratory of Clinical Science, National Institute of Mental Health, Bldg 10, 2D-47, Bethesda,

MD 20014 Introductory remarks at international symposium on "Non-striatal dopaminergic neurons." (Unpublished paper). DCBR, IRP, NIMH, 1976.

In a brief review on nonstriatal dopaminergic neurons, the following topics are discussed: 1) the findings which indicated the role of dopamine as a neurotransmitter; 2) the metabolic pathways by which dopamine is synthesized and metabolized; 3) the methods that made possible the rapid advances in the study of dopaminergic systems; 4) the dynamics of how drugs which act on the CNS affect dopamine metabolism in order to achieve their effects; and 5) the presence of dopamine in brain areas other than the nigrostriatal pathway. 20 references.

001882 Barton, Howard R. no address /Reply to a letter criticizing points in a letter on the neuromuscular side-effects of antipsychotics./ Dr. Barton replies. *American Journal of Psychiatry*. 133(9):1089-1090, 1976.

In a letter to the editor, reply is made to a criticism of a previous letter dealing with the neuromuscular side-effects of antipsychotics. Although amantadine does increase dopamine release in the animal brain and is useful in treating Parkinson's syndrome, in which dopamine availability appears to be diminished, the drug loses effectiveness after a few months. It is suggested that by increasing turnover of dopamine, amantadine ultimately reduces the functional and storage pool of dopamine in pallidostriatal tissue and may therefore ameliorate tardive dyskinesia. It is also stated that although the presence or absence of specific brain cell damage in tardive dyskinesia remains to be determined, it has been postulated (Hollister, 1975) that morphological damage to presynaptic membranes may occur, resulting in dopamine leakage which would create denervation supersensitivity to dopamine. At this point, dyskinesia may become severe and irreversible. 2 references.

001883 Bender, D. A. Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, London W1P 7PN, England Tryptophan and serotonin in schizophrenia. *Lancet* (London). No.7982:427, 1976.

In a letter to the editor, the correspondent agrees with the view of Smythies (*Lancet*, July 17, 1976, p. 136) that a defect of serotonergic systems is involved with schizophrenia. However, the correspondent disagrees with the suggestion that the defect may be one of serotonergic underactivity and proposes that the defect is one of overactivity. Research performed by the correspondent indicates that while patients were controlled by chlorpromazine or other antipsychotic drugs, their brain serotonin synthesis was apparently normal, but that after withdrawal of the drugs, serotonin synthesis in the brain increased at about the same time as exacerbation of schizophrenic symptoms occurred. It is suggested that chlorpromazine and other antipsychotic drugs may exert their beneficial effects in schizophrenia by blockade of the serotonin receptors in the central nervous system. 6 references.

001884 Bente, D.; Frick, K.; Lewinsky, M.; Penning, J.; Scheuler, W. Abteilung für Psychophysiologie, Freie Universität Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany /Signal analysis study of the effect of the antidepressant nomifensine on the EEG of healthy probands./ Signalanalytische Untersuchungen zur Wirkung des Antidepressivums Nomifensin auf das EEG gesunder Probanden. *Arzneimittel-Forschung* (Aulendorf). 26(6):1120-1125, 1976.

The effects of nomifensine, a new antidepressant, were studied on the EEG of 10 normal subjects. Subjects received

either placebo or 100mg nomifensine p.o. and EEG recording began 140 min later. Nomifensine caused a significant change in the EEG whereby an initial rise was followed by an oscillating decline. Alpha waves showed an increased level at first, and then decreased, showing wide oscillations while delta, theta, and beta 1-3 rhythms increased. Nomifensine caused a distinct shift in vigilance with two different partial processes. Following an initial stabilization of the alpha frequency, there was a polyrhythmic disintegration of the alpha rhythm with an increase in slower and faster frequencies. Simultaneously, a shift occurred within the beta range, resulting in an increase in the 23.5 to 32.0 Hz components. 11 references.

001885 Bente, D.; Frick, K.; Lewinsky, L.; Scheuler, W. no address A system for pattern-oriented spectral analysis of EEG data and its application in pharmacoelectroencephalography. *Electroencephalography and Clinical Neurophysiology* (Amsterdam). 41(6):666-667, 1976.

At a meeting of the German EEG Society in Munster in 1975, the design and function of a program system for processing and analyzing EEG data which can be used to assess and measure drug induced EEG changes were reported. The data are organized in such a way that: 1) the time course and dynamics of EEG patterning can be presented in chronospectrograms; 2) a great number of secondary parameters can be selected from spectral estimates to be statistically evaluated; and 3) the original time function is preserved and can be displayed in correspondence with interesting analysis epochs. As an example of the use of this system, the EEG effects produced in healthy volunteers by the antidepressant drug nomifensin were presented.

001886 Bianchi, G. N. Dept. of Psychological Medicine, Christchurch Clinical School, Christchurch, New Zealand The rational use of anxiolytics. *New Zealand Medical Journal* (Dunedin). 83(563):303-308, 1976.

Current knowledge on the characteristics of anxiolytics is reviewed, and it is noted that because the common symptoms of anxiety occur in a great array of illnesses, diagnosis is of first importance. If the anxiety state persists for a month or so, the illness might be termed an anxiety neurosis, and if there is no accompanying depression, a short course of benzodiazepine may be of value. With depression present to more than a mild degree as part of the neurosis, the tricyclic antidepressant doxepine usually achieves better results than benzodiazepine. Imipramine can be helpful for the phobic anxiety syndrome and monoamine oxidase inhibitors can be of separate utility. If the anxiety and depression occur in the context of alcoholism, thioridazine and amitriptyline have certain advantages.

001887 Bradlow, H. Leon; Boyar, Robert M.; O'Connor, John; Zumoff, Barnett; Hellman, Leon. Department of Oncology and Institute for Steroid Research, Montefiore Hospital and Medical Center, Bronx, NY 10467 Hypothyroid-like alterations in testosterone metabolism in anorexia nervosa. *Journal of Clinical Endocrinology and Metabolism*. 43(3):571-574, 1976.

The metabolism of ¹⁴C-testosterone was studied in eight severely underweight young women with anorexia nervosa. It is concluded that the data demonstrate that the low plasma triiodothyronine (T₃) concentrations in patients with anorexia nervosa may be related to the development of one of the characteristic biochemical abnormalities found in clinical hypothyroidism, namely a decreased Androsterone/etiocolanone ratio. It is also suggested that the "low T₃ syndrome" may be associated with biochemical hypothyroidism. 21 references. (Author abstract modified)

001888 Brazier, M. A. B.; Crandall, P. H.; Walsh, G. O. Dept. of Anatomy, Div. of Neurosurgery, University of California Medical Center, Los Angeles, CA Enhancement of EEG lateralizing signs in temporal lobe epilepsy: a trial of diazepam. *Experimental Neurology*. 51(1):241-258, 1976.

Reports are given of a subgroup of 13 patients with intractable epileptic seizures in whom unequivocal lateralizing signs were extremely difficult to obtain. On the basis that normal cerebral neurons react to intravenous diazepam by giving fast activity in the electroencephalogram (EEG), this simple test was given interictally in an attempt to differentiate, by computer analysis, normal and abnormal responses in the EEG. The results are reported for each patient in comparison with all other available lateralizing signs, clinical and electroencephalographic from scalp and deeply implanted electrodes, both ictally and interictally. Results indicate that the test was congruent with other EEG signs and that it can therefore be viewed as an additional source of lateralizing data. 25 references. (Author abstract modified)

001889 Breyer, U.; Petruch, F.; Gaertner, H. J.; Pflug, B. Institut für Toxikologie, Universität Tübingen, Wilhelmstrasse 56, D-7400 Tübingen, Germany /Thin layer chromatographic determination of plasma levels of tricyclic psychotropic drugs: initial results on a relationship to the clinical effect of neuroleptics./ *Dünnschichtchromatographische Bestimmung von Plasmaspiegeln tricyclischer Psychopharmaka: Erste Ergebnisse über eine Beziehung zur klinischen Wirkung von Neuroleptika*. *Arzneimittel-Forschung (Aulendorf)*. 26(6):1153, 1976.

Plasma levels of perazine, clozapine, amitriptyline, and imipramine and their metabolites were determined by thin layer chromatography followed by remission photometry in ultraviolet light. More than 100 psychiatric patients were studied. Large interindividual variations were found in plasma levels of drugs given in the same dose. Plasma levels of perazine and clozapine in acute schizophrenics were found to correlate with clinical improvement. In patients who were not responding to perazine, an increase in dose led to increased plasma levels and clinical improvement. In patients treated with clozapine, the relationship between plasma levels and clinical improvement was not as clearcut. 3 references.

001890 Burman, Kenneth D.; Dimond, Richard C.; Earll, Jerry M.; Wright, Frances D.; Wartofsky, Leonard. Department of Endocrinology and Metabolism, Walter Reed Army Medical Center, Washington, DC 20012 Sensitivity to lithium in treated Graves' disease: effects on serum T4, T3 and reverse T3. *Journal of Clinical Endocrinology and Metabolism*. 43(3):606-613, 1976.

Seven patients judged to be euthyroid following treatment of diffuse toxic goiter were studied to determine if they were susceptible to lithium induced hypothyroidism. These data suggest that patients euthyroid following treatment of diffuse toxic goiter display sensitivity to the antithyroid effects of lithium. Furthermore, these observations support the thesis that the inhibitory effects of lithium and iodine upon thyroid hormone synthesis or secretion may involve a similar mechanism of action since increased thyroidal iodine content may be a consequence of therapy with either agent. 38 references. (Author abstract modified)

001891 Byck, Robert. Department of Pharmacology, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 Peptide transmitters: a unifying hypothesis for euphoria, respiration, sleep, and the action of lithium. *Lancet* (London). No.7976:72-73, 1976.

A hypothesis is proposed that transmitter substances or modulator substances in the brain that have actions similar to morphine may control functions such as analgesia, sleep, euphoria, and depression of respiration in man. The hypothesis further proposes that enkephalin, a peptide, is a controlling neurotransmitter which by binding to opiate receptors, determines mood state and influences respiratory patterns and sleep patterns. Lithium may act through modification of the affinity of the opiate receptor for an endogenous morphine like substance. The theory predicts the blocking action of naloxone in mania and in most drug induced euphorias. A new chemical pathophysiological basis for mental illness is implied. 10 references. (Author abstract modified)

001892 Caldwell, John Department of Biochemical and Experimental Pharmacology, St. Mary's Hospital Medical School, London W2 1PG, England The placental transfer of drugs during childbirth: a possible influence on the newborn. *Journal of Psychosomatic Research (Oxford)*. 20(4):267-271, 1976.

A review of the literature regarding the use of analgesic drugs during delivery and their effect on the newborn is presented. The ideal analgesic is described as an analgesic that would not influence maternal consciousness and cooperation and also have no effect on the neonate. The pharmacological effect of analgesics used in childbirth on the newborn is extrapolated from their known effect in adults to the neonatal situation. Two possible mechanisms are discussed: 1) the effects may be due to the direct effects of the drug on the newborn; and 2) the effects may arise indirectly from changes in the physiology of the mother that can influence the newborn. It is concluded that there is a need for multidisciplinary research (pharmacological, psychological, and physiological) into the problem of placental transfer of drugs during delivery. 13 references.

001893 Candelise, L. Clinica delle Malattie Nervose e Mentali dell'Università di Milano, Milan, Italy /Haloperidol, reserpine, L-dopa and amantidine in the treatment of Huntington's chorea./ *Terapia della corea di Huntington. Azione del serenase, reserpina, L-dopa, amantadina sulle ipercinesie coreiche*. *Rivista di Patologia Nervosa e Mentale (Firenze)*. 96(1):54-63, 1975.

In a study of the function of catecholamine in extrapyramidal disease, six patients with chronic progressive hereditary Huntington's chorea, five females and one male, 32 to 81 years of age, were given two drugs that should reduce striatal dopamine activity, haloperidol and reserpine, and two drugs that should increase it, L-dopa and amantidine. Haloperidol was most effective in reducing hyperkinesia, followed by reserpine. Treatment with L-dopa had no appreciable effect on involuntary movements. Contrary to theoretical expectations, amantidine produced a slight improvement in the control of involuntary activity. 36 references. (Author abstract modified)

001894 Casey, Daniel E. Veterans Administration Hospital, Portland, OR Tardive dyskinesia: are there subtypes? *New England Journal of Medicine*. 295(19):1078, 1976.

In a letter to the editor the hypothesis that clinical tardive dyskinesia represents a defect in the balance between cholinergic and dopaminergic influences converging on the striatum is examined. Severe tardive dyskinesia was treated in 6 patients with challenge doses of a dopamine agonist (levodopa), an antagonist (droperidol), an acetylcholine agonist (physostigmine) and an antagonist (benztropine). All patients showed a change in dyskinesia with at least one of these agents. Patients were

then treated with dimethylaminoethanol (deanol) for 1 month: three improved; one showed no change; and two became worse. Decreased movement after droperidol or physostigmine characterized all three deanol improved subjects, whereas the three unimproved patients showed heightened dyskinesia with droperidol or physostigmine. Levodopa and benzotropine did not consistently alter the movements. Dopamine and acetylcholine influencing agents altered the movements. It is concluded that a subgroup has merged that seems to be opposite to the traditional pharmacologic theory of dopaminergic dominance or cholinergic deficit. 7 references.

001895 Casper, R. C.; Pandey, G.; Gosenfeld, L.; Davis, J. M. Illinois State Psychiatric Institute, 1601 West Taylor Street, Chicago, IL 60612 **Intracellular lithium and clinical response.** *Lancet* (London). No. 7982:418-419, 1976.

The relationship between intracellular (red blood cell, RBC) lithium levels and RBC/plasma lithium ratios and clinical response to lithium therapy was studied in 16 patients diagnosed as having schizoaffective or affective illnesses. The seven patients who responded well to lithium therapy and who could be maintained on lithium alone had substantially higher RBC/plasma ratios than the nine patients who responded poorly to lithium and required other medication. Some of the characteristics which may correlate with the ratios are discussed. 3 references.

001896 Christ, W.; Rakow, D.; Honecker, H.; Coper, H. Institut für Neuropsychopharmakologie, Freie Universität Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany **Determination of monoamine oxidase and catechol-O-methyltransferase in human blood components: methodological aspects.** *Bestimmung der Monoaminooxidase und Catechol-O-methyltransferase in menschlichen Blutbestandteilen: methodische Aspekte.* *Arzneimittel-Forschung* (Aulendorf). 26(6):1151-1152, 1976.

Catechol-O-methyltransferase (COMT) was determined in human erythrocytes and monoamine oxidase (MAO) was determined in human platelets. COMT was also determined in the human brain, and in rat erythrocytes, brain, and liver. The substrates used in the assay were 3,4-dihydroxybenzoic acid and 3,4-dihydroxybenzaldehyde. Km and the meta/para relationship of O-methylation were determined. MAO was assayed by tyramine, tryptamine, and phenylethylamine. For each substrate, the Km, Vmax, and IC-50 by tranylcypromine were determined. Platelets were taken from 14 healthy controls, and interindividual variations of the biochemical constants were very low. 7 references.

001897 Colson, James D. United States Air Force Biomedical Service Corps, Wilford Hall Medical Center, Lackland Air Force Base, TX **Prescription and nonprescription anorexiant.** *Journal of the American Pharmaceutical Association.* 16(10):565-567, 1976.

The use of prescription and nonprescription anorexiant for short-term treatment of endogenous obesity is discussed. A table of brand name legend anorexiant, generic composition and general remarks is given. These agents are all phenethylamine analogs and are thought to act on hypothalamic and limbic appetite regulation regions as well as stimulating the central nervous system. A tolerance to these agents will develop, often necessitating dosage increase which may result in a variety of sympathomimetic secondary side-effects. Chronic use may result in abnormal behavioral changes. Dependence liability and abuse potential of these agents is high; and in view of these risk factors, overall benefit is thought to be small. A table of nonprescription anorexiant giving brand

names, manufacturer, composition, and comments is presented and the mechanism of action of the major components of these drugs are discussed. It is concluded that although the effectiveness of these drugs in producing weight loss is limited and transitory without appropriate followup methods their psychological reinforcing and motivating value should not be overlooked. 13 references.

001898 Cooper, Thomas B.; Allen, David; Simpson, George M. Rockland Research Institute, Orangeburg, NY 10962 **A sensitive method for the determination of amitriptyline and nortriptyline in human plasma.** *Psychopharmacology Communications.* 2(2):105-116, 1976.

A highly sensitive and reproducible technique for the quantitation of amitriptyline and nortriptyline is described. Steady state data and data on amitriptyline levels and nortriptyline levels obtained following a single oral dose of amitriptyline are reported. Chlordiazepoxide, diazepam, and flurazepam ingestion was tested and found not to interfere with this procedure. 13 references. (Author abstract modified)

001899 Cooper, Thomas B.; Simpson, George M. Rockland Research Institute, Orangeburg, NY 10962 **The 24-hour lithium level as a prognosticator of dosage requirements: a 2-year follow-up study.** *American Journal of Psychiatry.* 133(4):440-443, 1976.

A technique whereby individual lithium dosage requirements can be predicted from 24 hour blood samples has been previously described and further experience over a 2 year period has shown the predictions to be reproducible over time. A micromethod for lithium determination is described, as are several cases in which aberrant results were found to indicate inadequate laboratory techniques or patients' failure to take medication. Because the technique reveals immediately those patients at the extremes of dosage ranges, toxicity and the need for frequent sampling can be avoided. 11 references. (Journal abstract modified)

001900 Crosignani, P. G.; D'Alborton, A.; Peracchi, M.; Reschini, E. Department of Obstetrics and Gynecology, University of Milan, I-20122 Milan, Italy **Dopamine-induced inhibition of prolactin secretion in amenorrhoea-galactorrhoea.** *Lancet* (London). No.7992:975, 1976.

It is suggested that dopamine infusion lowers the raised plasma prolactin levels in functional amenorrhoea-galactorrhoea. Although the level of dopamine action is still controversial, the blocking effect on the response of plasma thyroid stimulating hormone to thyrotrophin releasing hormone suggests a direct effect on the pituitary gland. 4 references.

001901 Cushman, Paul, Jr. Department of Medicine, St. Luke's Hospital Center, Columbia University, New York, NY 10025 **Cannabinols and the rosette forming properties of lymphocytes in vitro.** *Life Sciences* (Oxford). 19(6):875-886, 1976.

An in vitro study comparing the effects of tetrahydrocannabinol (THC), cannabinol (CBN), cannabidiol (CBD), and olivetol on the rosetting properties of T-cells was performed, and the effects of addition of THC to aliquots of lymphocytes obtained from marijuana smokers was also studied. Preincubation of lymphocytes with THC obtained from controls produced reduction in early but not total T-cell rosettes compared to aliquots treated with vehicle alone. Similar reductions in early rosettes were seen after preincubation with CBN, CBD, and olivetol. The marijuana smokers' lymphocytes were

less affected by preincubation with THC than those from controls. Presumably their lymphocytes may already have been affected by prior exposure to cannabinoids. These data show that THC and other cannabinoids can affect the rosetting properties of T-cells in vitro and may provide a model for the study of THC effects on these immunocompetent cells. 18 references. (Author abstract modified)

001902 Dalton, William S.; Martz, Robert; Rodda, Bruce E.; Lemberger, Louis; Forney, Robert, B. Department of Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, IN **Influence of cannabidiol on secobarbital effects and plasma kinetics.** *Clinical Pharmacology and Therapeutics*. 20(6):695-700, 1976.

To investigate the possible metabolic interaction between cannabidiol (CBD) and secobarbital, 6 male volunteers received 150mg/70 kg sodium secobarbital orally immediately after smoking a marihuana cigarette prepared to deliver a specific quantity of CBD. Clinical effects and plasma secobarbital concentrations were recorded at periodic intervals. CBD did not alter the summary parameters which describe the secobarbital plasma concentration time curve. Secobarbital half-life, peak concentration, time of peak concentration, and area under the curve were unchanged by the coadministration of CBD. Clinical effects of secobarbital were also unaltered by CBD pretreatment. Thus at the doses administered, CBD does not appear to inhibit secobarbital metabolism in man. 20 references. (Author abstract modified)

001903 Dawley, Harold H., Jr.; Ellithrope, Dean B.; Tretola, Rocco. Psychology Service, Veterans Administration Hospital, 1601 Perdido Street, New Orleans, LA 70146 **Aversive smoking: carboxyhemoglobin levels before and after rapid smoking.** *Journal of Behavior Therapy and Experimental Psychiatry*. 7(1):13-15, 1976.

Ten healthy subjects were tested before and after rapid smoking (one technique used in aversive smoking behavior therapy) to determine the carboxyhemoglobin levels in human arterial blood after rapid smoking. Possible subjects were rejected from the testing if they were not in good physical health, were significantly overweight, and were over 40 years old. Subjects were given an electrocardiogram to insure that only healthy subjects were tested. Analysis of the findings revealed in average increase of carboxyhemoglobin of 3.08%. Oximetrically determined oxygen saturation decreased an average of 5.58%. The data suggest significant decrease in arterial oxygen saturation following rapid smoking. The need for careful screening designed to rule out subjects prone to cardiovascular disease is stressed. 11 references. (Author abstract modified)

001904 De Lean, Jacques; Richardson, J. Clifford; Hornykiewicz, Oleh. Division of Neurology, 11 NUW, Toronto General Hospital, 101 College Street, Toronto, Ontario M5G 1L7, Canada **Beneficial effects of serotonin precursors in postanoxic action myoclonus.** *Neurology*. 29(9):863-868, 1976.

In two patients with postanoxic action myoclonus, L-tryptophan or an oxidase inhibitor induced a moderate improvement, but L-5-hydroxytryptophan had greater therapeutic effect. Methysergide, a potent blocker of serotonin receptors, consistently induced a marked deterioration in myoclonus. Pretreatment cerebrospinal fluid 5-hydroxyindoleacetic acid levels were reduced significantly in both patients. The findings suggest that postanoxic action myoclonus is associated with insufficient serotonergic activity in the central nervous system. 47 references. (Author abstract modified)

001905 Delong, A. F.; Smyth, R. D.; Polk, A.; Nayak, R. K.; Reavey-Cantwell, N. H. William H. Rorer, Inc., Research Division, 500 Virginia Drive, Fort Washington, PA 19034 **Blood levels of methaqualone in man following chronic therapeutic doses.** *Archives Internationales de Pharmacodynamie et de Therapie* (Ghent). 222(2):322-331, 1976.

Human serum was analyzed for methaqualone and hydroxylated metabolites by gas liquid chromatographic, ultraviolet spectrophotometric and spectrofluorimetric procedures. Intact methaqualone was found to be the major circulating drug component after administration of multiple 300mg daily doses over a 28 day period. Hydroxylated methaqualone metabolites, if present, were estimated to be in extremely low concentrations. After acute ingestion of large quantities of methaqualone, at least one methaqualone metabolite was present in serum obtained from subjects with a history of chronic drug abuse. 22 references. (Author abstract modified)

001906 Demisch, L.; Bochnik, H. J. Zentrum der Psychiatrie im Klinikum, Johann Wolfgang Goethe-Universität, Heinrich-Hoffmann-Strasse 10, D-6000 Frankfurt/Main, Germany **Improvement of lithium prophylaxis of endogenous phasic psychoses: aspects of parallel lithium determination in serum and in erythrocytes.** *Zur Verbesserung der Lithiumprophylaxe endogen phasischer Psychosen: Aspekte der parallelen Lithiumbestimmung im Serum und in Erythrozyten.* *Arzneimittelforschung* (Aulendorf). 26(6):1149-1151, 1976.

Lithium ion determination in red blood cells and in serum is discussed as a possible prophylactic in endogenous phasic psychoses. Lithium levels were determined in erythrocytes and serum of two groups of patients. One group of 16 patients, average age 43 years, had been on lithium 4 weeks. Their serum lithium level was 0.77mEq/l, and the erythrocyte lithium level was 0.30mEq/l, giving an erythrocyte/serum ratio of 0.39. Another group of 42 patients, average age 45 years, had been on lithium at least one year, average 3.3 years. Their serum lithium level was 0.81mEq/l, and their erythrocyte lithium level was 0.40mEq/l, giving an erythrocyte/serum ratio of 0.49. In 30% of the patients, the erythrocyte lithium level was a more reliable indicator of clinical response and risk of toxicity than was the serum lithium level. Erythrocyte/serum lithium ratios do not differ between unipolar, bipolar, and schizoaffective patients. Low lithium erythrocyte/plasma ratios correspond with low MAO activity in platelets. 9 references.

001907 Dick, Pierre. Clinique Universitaire de Psychiatrie (Bel-Air) CH-1225 Chene-bourg, Geneva, Switzerland **Distribution of Li in the CNS and the function of biological clocks.** *Repartition du Li dans le S.N.C. et fonctionnement des horloges biologiques?* *Evolution Psychiatrique* (Toulouse). 41(3):611-617, 1976.

The rate of absorption of lithium in different parts of the body as evidence of an existing biological timetable for each organ is investigated. Studies of the peculiarities of penetration and concentration of lithium and the diverse physical chemical factors in the tissues of the body are described. Studies of lithium absorption in the brain of rats and humans show different levels, with an accumulation at sites rich in monoamines. Results of chronobiological studies show various biochemical parameters of the body in the efficiency of medication. Examples of chronopharmacology in manic-depressive psychosis and catatonic states are given. 16 references.

001908 Elley, J. H.; Hansen, C. Eggert; Larsen, N.-E.; Naestoft, J. Slostrup, Denmark **Clinical aspects of kinetic studies on perphenazine.** *Acta Psychiatrica Scandinavica* (Kobenhavn). Supplement 265:22, 1976.

A summary of a report on plasma concentrations of Perphenazine and Perphenazinesulphoxide by gas chromatography after various administration forms in patients and healthy volunteers, given at a symposium on psychiatric prevention and crisis intervention held in June 1976 at Turku, Finland, is presented. Intravenously administered, the drug showed exponential elimination from plasma and a plasma half-life of approximately 9.5 hours. After chronic oral medication, the systemic availability seemed poor, presumably due to a considerable first pass effect. Side-effects were often associated with high concentrations in plasma, but occurred even at low concentrations. Consequences of these clinical kinetic findings for clinical use are discussed.

001909 Enna, S. J.; Bennett, J. P., Jr.; Burt, D. R.; Creese, I.; Snyder, Solomon H. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Stereospecificity of interaction of neuroleptic drugs with neurotransmitters and correlation with clinical potency.** *Nature (London)*. 263(5575):338-341, 1976.

Using binding techniques to study neurotransmitter receptors directly, studies were undertaken to determine how reliably stereospecificity and correlations between clinical and biochemical effects can reveal the biochemical basis of neuroleptic drug action. The results suggest that although these criteria are valuable, they can obfuscate rather than clarify drug mechanisms if not used carefully. Of the several biochemical effects of neuroleptics, blockade of dopamine receptors best accounts for therapeutic effects of both butyrophenone and phenothiazine neuroleptics. 32 references.

001910 Extein, Irl; Van Woert, Melvin H.; Roth, Robert H.; Bowers, Malcolm B., Jr. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 14C-Homovanillic acid in the cerebrospinal fluid of Parkinsonian patients after intravenous 14C-L-dopa. *Biological Psychiatry*. 11(2):227-232, 1976.

Applicability in humans of a modification of probenecid accumulation in cerebrospinal fluid (CSF) of endogenous homovanillic acid (HVA), a major metabolite of brain dopamine was tested. Six patients with Parkinson's disease and five controls were premedicated with probenecid and the peripheral decarboxylase inhibitor alpha-methyldopahydrazine (Carbidopa) before intravenous administration of 50 micrograms of 14C-L-dopa in tracer quantity. Seven and one half hours later lumbar CSF was obtained. 14C-Homovanillic acid a major metabolite of brain dopamine, was isolated by thin layer chromatography and measured. The statistically significant positive correlation between endogenous HVA and 14C-HVA in the entire patient group and the slightly lower values of endogenous HVA and 14C-HVA in the CSF of the parkinsonians support the assumption that the concentration of HVA in the CSF after probenecid treatment reflects brain dopamine turnover. Measurement of labeled HVA here seems to have little advantage over measurement of endogenous HVA alone. 21 references. (Author abstract)

001911 Forsman, Anders; Ohman, Rolf. Department of Psychiatry III, Lillhagen's Hospital, University of Goteborg, Sweden **Pharmacokinetic studies on haloperidol in man.** *Current Therapeutic Research*. 20(3):319-336, 1976.

The pharmacokinetics of haloperidol in man was studied after intravenous (iv) administration and after oral administration. Various pharmacokinetic parameters were computed assuming one compartment to three compartment open models. The serum half-life ranged from 10.1 hours to 19 hours after iv administration and from 12 hours to 38.3 hours after oral ad-

ministration. The bioavailability was in order of 60% and distribution volume was approximately 1300 liters. Evidence of enterohepatic recirculation and some extrahepatic metabolism of the drug was found. It is suggested that these results can explain individual variability in the response to haloperidol and varying clinical effects occurring with different methods of administration of haloperidol. 17 references. (Author abstract modified)

001912 Gaillard, Anthony W. K.; Trumbo, Don A. Institute for Perception, Kampweg 5, Soesterberg, The Netherlands **Drug effects on heart rate and heart rate variability during a prolonged reaction task.** *Ergonomics (London)*. 19(5):611-622, 1976.

The effects of an amphetamine and a barbiturate on heart-rate and heart-rate variability were investigated during long-term performance. Subjects worked for 3 hours in a serial reaction test, which included blocks with variable or constant interstimulus intervals (ISI). Besides the interbeat interval (IBI), derived from the successive R-peaks of the ECG, the variability of IBI was scored in three ways. Each of these four scores increased as a function of time on task, indicating a gradually decreasing activation level during the 3 hour session. Amphetamine had an activating effect, decreasing both IBI and IBI variability; the barbiturate effect on the other hand was paradoxical: this drug tended to increase IBI variability, but to decrease IBI. The IBI changes between constant and variable blocks were neglectable after amphetamine, while these changes were pronounced after barbiturate treatment. IBI variability was reduced during blocks with variable ISIs, where mental effort was assumed to be maximal. This reduction in variability was larger for amphetamine and tended to be smaller for barbiturate as compared to the placebo condition. 16 references. (Author abstract)

001913 Gero, Alexander. Department of Pharmacology, Hahnemann Medical College, Philadelphia, PA 19102 **Inactivity of enkephaline on human serum esterase.** *Life Sciences (Oxford)*. 19(4):479-481, 1976.

In view of the recent discovery of enkephaline, an endogenous substance which, like morphine and other opioid drugs, depresses electrically induced contractions of the guinea pig ileum, an attempt was made to determine if it behaves as an opiate on human serum esterase as well. It was found that while opioid agonists accelerate the hydrolytic action of human serum esterase, and opioid antagonists competitively antagonize this acceleration, the endogenous morphine like factor methionine/enkephaline neither accelerates the enzyme nor competes with an opioid accelerator. It is proposed that the pentapeptide enkephaline is only the prosthetic group of the true endogenous morphine like factor and too short a peptide chain to have a stable enough secondary structure for opioid action in the presence of dissolved protein. 6 references. (Author abstract modified)

001914 Greenblatt, David J.; Schillings, Roger T.; Kyriakopoulos, Adrian A.; Shader, Richard I.; Sisenwine, Samuel F.; Knowles, John A.; Ruelius, Hans W. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Clinical pharmacokinetics of lorazepam: 1. absorption and disposition of oral 14C-lorazepam.** *Clinical Pharmacology and Therapeutics*. 20(3):329-341, 1976.

Biotransformation of a pharmacologically inactive glucuronide metabolite was found to be the major mechanism of lorazepam clearance. Eight healthy male subjects received single 2mg oral doses of lorazepam containing 24 micrograms

Ci/mg of 2-14C-lorazepam. Multiple venous blood samples were drawn during the first 96 hours after the dose, and all urine and stool were collected for 120 hours after dosing. Concentrations of lorazepam and its metabolites in body fluids were determined by appropriate analytic techniques. The apparent elimination half-life of lorazepam was about 12 hours. A mean of 88% of administered radioactivity was recovered in urine, and 7% was recovered in stool. Lorazepam glucuronide comprised 86% of urinary reactivity; its renal clearance was 37 ml/min. Other identified metabolites included hydroxylorazepam, a guinazolinone derivative, and a guinazoline carboxylic acid; all of these were quantitatively minor. 42 references. (Author abstract modified)

001915 Greil, W.; Eisenried, F.; Duhm, J. Psychiatrische Universitätsklinik, Nussbaumstrasse 7, D-8000 Munich 2, Germany / **Distribution of lithium between erythrocytes and plasma: in vitro study of the transport of lithium into human erythrocytes.** / Über die Verteilung von Lithium zwischen Erythrozyten und Plasma: In-vitro-Untersuchung zum Transport von Lithium an menschlichen Erythrozyten. *Arzneimittelforschung* (Aulendorf). 26(6):1147-1149, 1976.

Distribution of lithium ion between red blood cells and plasma was studied. In 30 ambulatory patients who had been treated with lithium for at least a year, the intra/extracellular lithium quotient varied between 0.19 and 0.70. Erythrocytes were removed from heparinized blood of lithium treated and healthy subjects and placed in a saline solution. In the lithium uptake study, extra/intracellular quotients ranged from 0.16 (in the 0.5mM suspension) to 0.33 (in the 5mM suspension). In the lithium release experiments, lithium ion was released from cells into the medium. The results showed that lithium could be released against an electrochemical gradient. Release of Li was inhibited by replacing extracellular Na with K or choline, but was not affected by ouabain or glucose depletion, thus giving no proof for active lithium transport. 6 references.

001916 Gruen, Peter H.; Sachar, Edward J. no address **Prolactin secretion and antipsychotic efficacy.** *American Journal of Psychiatry*. 133(9):1090, 1976.

In a letter to the editor, the results of an investigation into the ability of several psychoactive drugs to stimulate prolactin secretion in humans is reported. Molindone, loxapine, chlorpromazine, butaperazine, thioridazine, and haloperidol all stimulated prolactin secretion. Nonantipsychotic phenothiazines such as promethazine, and other psychoactive drugs without antischizophrenic properties, such as diazepam, amitriptyline and lithium did not stimulate prolactin secretion. Since it appears that all currently available classes of antipsychotic drugs stimulate prolactin secretion by blocking its inhibition by dopamine, it is suggested that neuroleptic induced prolactin secretion in man be included in the evaluation of antidopaminergic properties of potentially efficacious antipsychotic drugs. 2 references.

001917 Guazzi, M.; Fiorentini, C.; Polese, A.; Olivari, M. T.; Magrini, F. Istituto Ricerche Cardiovascolari, Via Francesco Sforza, 35, I-20122 Milano, Italy **Antihypertensive action of propranolol in man: lack of evidence for a neural depressive effect.** *Clinical Pharmacology and Therapeutics*. 20(3):304-309, 1976.

The hypothesis that a neural depressive action is related to the antihypertensive effects of beta blockers is evaluated in 14 essential hypertensive male patients through the circulatory response to noxious stimuli. The pressor reaction to mental arithmetic was primarily mediated by cardiac stimulation (beta

receptors activation), that to cold by vasoconstriction (alpha receptors activation). Arithmetic and cold were tested to separate the effects of peripheral beta blockade from possible neural and other influences. Administration of propranolol yielded the following results: 1) the baseline pressure was reduced; 2) appearance, peak, and disappearance time of the circulatory reaction to either stimulus was not altered; 3) the pressor effect of arithmetic was decreased in an extent proportional to the reduced rise of cardiac output; and 4) pressure during cold reached the pretreatment levels through an augmented increase of vascular resistance. It is concluded that propranolol depresses only the circulatory reactions mediated through beta receptors activation and provide no evidence of effects other than beta blockade. 15 references. (Author abstract modified)

001918 Hinrichs, H.; Kunkel, H.; Luba, A.; Niethardt, P.; Reinhardt, B. no address **Psychophysiological aspects in EEG analysis of cerebral drug effects.** *Electroencephalography and Clinical Neurophysiology* (Amsterdam). 41(6):660-661, 1976.

At a 1975 meeting of the German EEG Society in Munster, a study on the relationship between the effects of drugs on the EEG and the behavioral characteristics of the subject was discussed. Proband with high neuroticism scores exhibited quantitatively different effects as well as qualitatively different and strongly contrasting EEG profiles in response to administration of pyritinol and to EMD 21.657 than did subjects with low neuroticism scores. It is suggested that EEG analyses which neglect interfering psychological variables may result in erroneous drug classifications. The findings support the idea that a direct relationship exists between brain function and behavior.

001919 Janowsky, David S.; Meacham, Martin P.; Blaine, Jack D.; Schoor, Michael; Bozzetti, Louis P. Department of Psychiatry, University of California, San Diego, School of Medicine, La Jolla, CA **Marijuana effects on simulated flying ability.** *American Journal of Psychiatry*. 133(4):384-388, 1976.

The effects of marijuana intoxication on the ability of ten certified airplane pilots to operate a flight simulator were studied. A randomized double-blind crossover design was used to compare the effect of active versus placebo marijuana. It was found that all ten pilots showed a significant decrease in measurements of flying performance 30 minutes after smoking active marijuana. For a group of six pilots tested sequentially for 6 hours, a nonsignificant decrease in flying performance continued for 2 hours after smoking the active drug. It was concluded that the effects of marijuana on flying performance may represent a sensitive indicator of the drug's psychomotor effects. 15 references. (Journal abstract modified)

001920 Jones, D. P.; Binnie, C. D.; Brown, R. L.; Lloyd, D. S. L.; Watson, B. W. Departments of Neurophysiology and Medical Electronics, St. Bartholomew's Hospital, London EC1A 7BE, England **The contingent negative variation and psychological findings in chronic hepatic encephalopathy.** *Electroencephalography and Clinical Neurophysiology* (Amsterdam). 40(6):661-665, 1976.

Using morphine as a provocative agent, any resulting change in cerebral function was assessed by measurement of the contingent negative variation (CNV) in conjunction with a psychological trail test in order to determine the usefulness of this procedure in the early diagnosis of chronic hepatic encephalopathy (CHE). Of the 26 subjects 6 tested had clinically overt CHE. A significant correlation between the change in CNV amplitude with morphine and the initial CNV amplitude,

consistent with the theoretical model of Tecce (1972), was found. However, the CNV and trail test results taken as a whole did not identify even those patients with overt CHE. It is concluded that the detection of differing degrees of latent CHE by this method is unlikely. 9 references. (Author abstract modified)

001921 Klotz, U.; Antonin, K.-H.; Bieck, P. R. Auerbachstr. 112, D-7000 Stuttgart, Germany **Pharmacokinetics and plasma binding of diazepam in man, dog, rabbit, guinea pig and rat.** *Journal of Pharmacology and Experimental Therapeutics*. 199(1):67-73, 1976.

The pharmacokinetics and plasma binding of diazepam (D) and its major metabolite, desmethyldiazepam, were compared in man, dog, rabbit, guinea-pig and rat. It is indicated that an unbound drug is rate determining for clearance by the liver, and that D fits into the restrictive elimination class in man. In the four animal species tested, plasma clearance was a direct linear function of the body surface area. A considerably higher extraction ratio than the unbound fraction of diazepam existed in the animal species, and blood clearance exceeded liver blood flow, giving reason to assume a much higher ability of the liver to metabolize D, and a species dependent extrahepatic metabolism. The large variations described suggest that pharmacokinetic data or plasma binding results cannot simply be extrapolated to man. 20 references. (Author abstract modified)

001922 Korf, J.; Sebens, J. B.; Venema, K.; van Praag, H. M. Department of Biological Psychiatry, Psychiatric University Clinic, Oostersingel 59, Groningen, The Netherlands **Serum levels of 5-hydroxyindole derivatives after administration of L-5-hydroxytryptophan ethyl ester.** *Research Communications in Chemical Pathology and Pharmacology*. 15(1):171-182, 1976.

The metabolism of 5-hydroxytryptophan ethyl ester (5-HTPE) was investigated using semiautomated methods, which are described, for the estimation of 5-hydroxyindole derivatives. Serum levels of 5-HTPE, 5-hydroxytryptophan, (5-HTP), 5-hydroxytryptamine (5-HT), and 5-hydroxyindole-acetic acid (5-HIAA) were measured after intravenous infusion of L-5-HTPE to humans. The levels of 5-HTP increased during the infusion but dropped rapidly when the intravenous infusion was terminated. Serum levels of 5-HIAA increased and remained constant for at least 6 h, suggesting that 5-HIAA is formed from the 5-HT stored in peripheral tissue or central tissue. Serum levels of 5-HIAA may be indicative of changes of 5-HT metabolism during drug treatment. Levels of 5-HTP may be used for the estimation of the availability of the ethylester of 5-HTP. 20 references. (Author abstract modified)

001923 Korsgaard, S. County Hospital, DK-4760 Vordingborg, Denmark **Baclofen (Lioresal) in the treatment of neuroleptic-induced tardive dyskinesia.** *Acta Psychiatrica Scandinavica* (Kobenhavn). 54(1):17-24, 1976.

A double-blind crossover study of the effects of baclofen and placebo was done on 20 female inpatients suffering from neuroleptic induced tardive dyskinesia. After 14 days of treatment 15 patients showed improvement on baclofen, whereas none showed improvement on placebo. Side-effects, though temporary, were observed in the form of sedation, muscular hypotonia, dizziness, vomiting, and muscular rigidity, and depression in one patient. Baclofen and other GABA ergic drugs used in the treatment of dyskinesia do not increase dopaminergic hypersensitivity, which is part of the pathogenesis of these conditions. GABA ergic therapy therefore is thought to be preferable in treatment of these conditions to

therapy with dopamine receptor blocking drugs. 20 references. (Author abstract modified)

001924 Koukkou, Martha; Lehmann, D. Forschungsdirektion der Psychiatrischen Universitätsklinik, Zurich, Switzerland **Human EEG spectra before and during cannabis hallucinations.** *Biological Psychiatry*. 11(6):663-677, 1976.

In a study of the characteristics of the EEG during cannabis induced hallucinations—experiences of compelling sensory percepts without external input — EEG correlates of subjective experiences induced by delta-9-trans-tetrahydrocannabinol (THC) and EEG correlates of individual disposition to such experiences were investigated. Twelve normal volunteers took THC orally. The subjects were asked to signal subjective experiences. The EEG was analyzed before and repeatedly after THC ingestion, during resting, attention, eye closure, visual hallucinations, and body image disturbances. EEG frequency spectra differed significantly between resting and visual hallucinations and body image disturbances. The differences included slower alpha and more theta during THC experiences, reminiscent of initial drowsiness EEG, and of some results in schizophrenia. The differences between spectra during visual hallucinations and during body image disturbances indicate different functional brain states. Subjects with a high tendency to cannabinol induced experiences exhibited resting spectra before and after THC with higher modal alpha frequencies (reminiscent of subjects with high neuroticism scores) than subjects with a low tendency. 32 references. (Author abstract modified)

001925 Kunkel, H. Abt. f. Klinische Neurophysiologie und Experimentelle Neurologie, Mediz. Hochschule Hannover, Postfach 180, 3-Hannover-Kleeefeld, Germany **EEG spectral analysis of the effects of caffeine./ EEG-Spektralanalyse der Coffein-Wirkung.** *Arzneimittel-Forschung* (Aulendorf). 26(3):462-465, 1976.

The central stimulating effect of caffeine may be quantified using EEG spectral analysis. Comparison of the effects of regular coffee and decaffeinated coffee with caffeine solution and placebo showed negligible intragroup differences in EEG, but highly significant intergroup differences. It may be concluded that caffeine is the effective factor. This study gives no valid evidence confirming possible effects of other coffee ingredients. 9 references. (Author abstract modified)

001926 Lader, M. H. no address **How tranquilizers work.** *British Journal of Hospital Medicine* (London). 16(6):622, 625-628, 1976.

The way in which the major tranquilizers work is reviewed. Despite intensive clinical usage of the major tranquilizers for 20 years and of the sedative tranquilizers for 15 years, the modes of action of these psychotropic agents are unknown. Recently, however, the evidence suggesting that major tranquilizers act by dopaminergic blockade has become compelling if not conclusive. The action of the barbiturates and the benzodiazepines may be particularly selective on the limbic system (amygdalohippocampal projections) and/or the ascending reticular activating system (noradrenergic neurones of the locus coeruleus). Meanwhile, slowly accumulating data on the pharmacokinetics of the tranquilizers facilitates more effective use in the clinic. 16 references. (Author abstract)

001927 Markianos, E. S.; Nystrom, I.; Reichel, H.; Matussek, N. Psychiatrische Klinik der Universität München, Nussbaumstrasse 7, D-8000 München 2, Germany **Serum dopamine-beta-hydroxylase in psychiatric patients and normals: effect of d-**

amphetamine and haloperidol. Psychopharmacology (Berlin). 50(3):259-267, 1976.

The effects of d-amphetamine and haloperidol on the serum dopamine-beta-hydroxylase activity in groups of normals and of psychiatric patients was studied using a thin layer radiochromatographic method. The percentage of patients with schizophrenic and with depressive symptomatology was higher in the population with high enzyme activities. In addition, d-amphetamine given to normals caused an increase in the serum activity while haloperidol caused the opposite effect. The activity in serum is interpreted as a loss in the enzyme from the place it acts physiologically, with possible influence on the noradrenaline synthesis rate. 29 references. (Author abstract)

001928 Martin, William R. National Institute on Drug Abuse, Addiction Research Center, P. O. Box 12390, Lexington, KY 40511 **Drugs five years later: naloxone.** Annals of Internal Medicine. 85(6):765-768, 1976.

The history, theory and use of the narcotic analgesic naloxone HCl is reviewed from a clinical and experimental perspective. Narcotic analgesics and related drugs act as agonists on several receptors that are responsible for their effects on pain perception, mood and feeling state, and respiration, as well as other pharmacologic actions. Naloxone is the first discovered antagonist that is devoid of agonistic activity and appears to be a competitive antagonist at several receptors. The ability of naloxone to displace or prevent the binding of agonistic narcotic is partly responsible for its antagonistic effects. The ability of naloxone to rectify narcotic depressed homeostats and precipitate abstinence is also related to its antagonistic activity. Certain cautions and principles are noted in the use of naloxone in treating narcotic overdose, reversing surgical analgesia, and the treatment of neonates and children. Unapproved uses of naloxone include reversing the psychotomimetic effects of certain agonists/antagonists, terminating narcotic induced convulsions and coma, reversing nonnarcotic depression, diagnosing physical dependence, and treating narcotic addicts. 25 references. (Author abstract modified)

001929 Møllerup, E. T.; Lauritsen, B.; Dam, H.; Rafaelsen, O. J. Psychochemistry Institute, Rigshospitalet, 9 Blegdamsvej, DK-2100, Copenhagen Ø, Denmark **Lithium effects on diurnal rhythm of calcium, magnesium, and phosphate metabolism in manic-melancholic disorder.** Acta Psychiatrica Scandinavica (Kobenhavn). 53(5):360-370, 1976.

The diurnal rhythm of plasma phosphate, calcium, and magnesium was studied in 34 lithium treated patients, in 42 other psychiatric patients, and in 47 healthy persons. During the 24 hour period, 17 blood samples were drawn from each patient. Lithium was given at 10 p.m. and in the next few hours plasma phosphate decreased compared with the two control groups. In the same period plasma calcium showed a temporary increase, whereas plasma magnesium was increased during the whole 24 hour period. The lithium treated patients had a reduced urinary calcium excretion during the night, and an increased urinary magnesium excretion during the day, whereas no changes were found in urinary phosphate excretion. 35 references. (Author abstract)

001930 Mirin, Steven M.; Mendelson, Jack H.; Ellingboe, James; Meyer, Roger E. Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, MA 02178 **Acute effects of heroin and naltrexone on testosterone and gonadotropin secretion: a pilot study.** Psychoneuroendocrinology (Oxford). 1(4):359-369, 1976.

The effects of opiates on pituitary gonadotropins — leutinizing hormone (LH) and follicle stimulating hormone (FSH) — and on the primary secretions of the end organs they influence were studied. Two detoxified male heroin addicts were given 10mg of intravenous heroin and experienced a rapid fall in plasma LH. FSH levels were unchanged. Approximately 4 hr after LH suppression by heroin, plasma testosterone levels also dropped markedly. Naltrexone pretreatment prevented opiate induced suppression of both LH and testosterone. Instead, an increased number of secretory bursts of LH occurred after naltrexone administration, and mean plasma LH levels were higher than those obtained during a saline control period. Testosterone and FSH secretion were not appreciably affected by naltrexone treatment. 24 references. (Author abstract modified)

001931 Misra, Anand L.; Vadlamani, Narasimhan L. New York State Office of Drug Abuse Services, Testing and Research Laboratory, Brooklyn, NY 11217 **Molecular complexes of cocaine, its active metabolites and some other stimulants with thiamine.** Research Communications in Chemical Pathology and Pharmacology. 15(2):401-404, 1976.

Ultraviolet spectroscopy was applied to study the molecular complexes of cocaine, its active metabolites, and some other stimulants with thiamine. All prepared compounds and complexes were measured in aqueous solutions at an ambient temperature in a spectrophotometer. The same concentration of drugs present in the complex studied was used in the reference cuvette in the spectral determinations of complexes. Results showed that cocaine, its pharmacologically active metabolites (norcocaine, benzoynorecgonine, and benzoylecgonine), and other central nervous system stimulants (dextrococaine, nicotine, caffeine, and p-hydroxy norephedrine) formed molecular complexes with thiamine. Implications of this interaction are for producing changes in electron structures, leading to alterations in the electrical character of the axonal membrane and resultant stimulatory response. 19 references. (Author abstract modified)

001932 no author. no address **Gluten and schizophrenia.** Lancet (London). No. 7964:844, 1976.

Observations are made on the relation of gluten (or cereal based foods) to adverse effects on schizophrenic patients as recorded by some researchers who conducted experiments regarding the administration of gluten. Another explanation which may account for these observed effects is that gluten may inhibit the absorption of tranquilizers and lead to altered plasma levels. 10 references.

001933 Ohlin, P.; Lundh, B.; Westling, H. Dept. of Clinical Physiology, University of Lund, Lasarettet, S-22185 Lund, Sweden **Carbon monoxide blood levels and reported cessation of smoking.** Psychopharmacology (Berlin). 49(3):263-265, 1976.

The carboxyhemoglobin (COHb) level was estimated in patients attending an antismoking clinic in an attempt to detect discrepancies between reported and actual smoking. A surprisingly large fraction of patients that reported "no smoking" were found to have abnormally high COHb. We believe that this discrepancy is due to the patients not reporting their smoking habits correctly. This phenomenon is further evidence that smoking should be regarded as a form of drug addiction in some persons. Some early relapses in stop smoking programs can apparently be explained by the patient's admitting previously concealed smoking. For scientific purposes the results of stop smoking cures should be evaluated by other means than the patient's own reports. 7 references. (Author abstract modified)

001934 Ortega, Eduardo; Rodriguez, Consuelo; Strand, L. James; Segre, Eugene. SA and Syntex Research, Palo Alto, CA **Effects of cloprednol and other corticosteroids on hypothalamic-pituitary-adrenal axis function.** *Journal of International Medical Research* (Northampton). 4(5):326-337, 1976.

The effects of cloprednol and other synthetic corticosteroids on hypothalamic pituitary adrenal (HPA) function were studied in healthy subjects after administration of a single oral dose of corticosteroid at 6 a.m. or 6 p.m. and after daily 6 a.m. administration of corticosteroids at various doses for 7 days. The degree of HPA suppression was assessed by metyrapone tests (METP), insulin hypoglycaemia tests (IHT) and 6 a.m. fasting plasma cortisol concentrations. Regardless of the corticosteroid tested, 6 p.m. dosing least four fold more suppressive of METP response than 6 a.m. administration. At therapeutically equivalent doses single doses of triamcinolone and dexamethasone were more suppressive of HPA axis function than cloprednol, hydrocortisone or prednisolone. After 6 a.m. administration for 7 days, 12.5mg of cloprednol did not impair the cortisol response to IHT or interfere with the METP response. The clinically equivalent dose of prednisolone (25mg) resulted in slightly greater HPA axis suppression. All doses of dexamethasone (0.5, 3.75 and 6.0mg) and of betamethasone (2.0, 4.0 and 6.5mg) were more suppressive of HPA axis function than either cloprednol or prednisolone. These results suggest that a equipotent antiinflammatory doses, cloprednol is slightly less suppressive of HPA axis function than prednisolone, and both cloprednol and prednisolone are much less suppressive than dexamethasone or betamethasone. 23 references. (Author abstract)

001935 Perel, J. M.; Mendlewicz, J.; Shostak, M.; Kantor, S. J.; Glassman, A. H. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Plasma levels of imipramine in depression: environmental and genetic factors.** *Neuropsychobiology* (Basel). 2(4):193-202, 1976.

Environmental and genetic factors influencing plasma levels of imipramine in depressed patients were investigated. On the basis of tentative evidence obtained from the study of 26 patients with unipolar affective illness, the variability in the response to imipramine is mostly due to interindividual differences in hydroxylating microsomal enzymes which are genetically controlled but whose activities are subject to modification by environmental factors such as overall pharmacological exposure and tobacco smoking. Additional significant pharmacodynamic variability (twofold) was found in the range of the volumes of distribution of imipramine in the patients. Clinical outcome was unequivocally related to plasma level. Unipolar nondepressive patients with levels less than 180ng/ml had a low probability of recovery, while levels above 180ng/ml were associated with a high probability of recovery. Unlike the findings of investigators working with nortriptyline, the data do not suggest an upper limit on plasma levels beyond which clinical response deteriorates. It appears that, on the basis of family studies, similar genetic properties lead to imipramine response among unipolar depressives. 18 references. (Author abstract modified)

001936 Poust, Rolland I.; Mallinger, Alan G.; Mallinger, Joan; Himmelhoch, Jonathan M.; Hanin, Israel. Department of Pharmacology, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15261 **Pharmacokinetics of lithium in human plasma and erythrocytes.** *Psychopharmacology Communications*. 2(2):91-103, 1976.

The time course of lithium concentration in plasma and red blood cells (RBCs) was measured in normal adult males fol-

lowing administration of single doses and multiple doses of lithium carbonate. From the single dose profiles, it was determined that lithium distribution between plasma and RBCs is not a simple partitioning phenomenon. The single dose time course measurements in both blood components were fit to a two compartment pharmacokinetic model in which the plasma was representative of the central compartment and the RBCs were representative of the tissue compartment. The importance of correcting for trapped plasma volume in studies measuring lithium RBC kinetics was emphasized. It was also demonstrated that one can accurately predict plasma and RBC lithium concentrations which are observed following multiple dosing, on the basis of single dose parameters obtained in the same subject. 22 references. (Author abstract)

001937 Roth, J. A. Department of Pharmacology and Therapeutics, School of Medicine and Dentistry, State University of New York at Buffalo, Buffalo, NY 14214 **Evidence for a single catalytic binding site on human brain type B monoamine oxidase.** *Journal of Neurochemistry* (Oxford). 27(5):1107-1112, 1976.

An investigation to determine whether the properties of human brain monoamine oxidase (MAO) resemble those of human platelet MAO and to determine whether multiple catalytic sites exist on the B form of brain MAO was conducted. Amitriptyline inhibited the B form of brain MAO under normal atmospheric conditions in a noncompetitive manner when phenylethylamine (PEA) was used as substrate and competitively when benzylamine was used as substrate. PEA and benzylamine inhibited each other's degradation noncompetitively. Pargyline and clorgyline were used to further distinguish whether PEA and benzylamine bind to different catalytic binding sites. The degree to which pargyline and clorgyline inhibited PEA or benzylamine deamination was essentially identical. When incubations were performed at elevated oxygen concentrations, PEA and benzylamine became mutually competitive inhibitors of each other's metabolism and amitriptyline inhibition of PEA deamination approached a competitive manner. It is suggested that PEA and benzylamine share a common catalytic binding site on the B form of MAO and bind to an inhibitory site on the reduced form of the enzyme. It is also suggested that amitriptyline binds to both the oxidized form and the reduced form of human brain type B MAO. 24 references. (Author abstract modified)

001938 Savary, Francois; Karassik, Steven; Gast, Joseph. Veterans Administration Hospital, Long Beach, CA **A comparative evaluation of the antipsoriatic effect of L-DOPA versus placebo in psoriasis.** *Current Therapeutic Research*. 20(2):130-133, 1976.

The effect of L-dopa in the treatment of psoriasis was measured by means of a double-blind crossover study with placebo in 35 volunteer subjects with chronic psoriasis. L-dopa administration resulted in beneficial effects in most of the psoriatic patients. Eight patients showed total improvement with complete remission during the study. Fourteen patients demonstrated partial improvement. Thirty patients experienced no adverse effects from L-dopa, and demonstrated definite improvement of their skin disease. The results in all 30 of these patients have made them eager to continue treatment because of their physical and emotional well being. 5 references. (Author abstract modified)

001939 Schiff, A. A. E. R. Squibb and Sons Ltd., Twickenham TW1 3QT, England **Do tricyclic antidepressants work?** *Lancet* (London). No.7976:106, 1976.

The theory that the antidepressant effect of amitriptyline may actually be due to its metabolite nortriptyline and that amitriptyline may merely act as a precursor of the true antidepressant substance is presented. 1 reference.

001940 Schmidt, Dieter. Klinikum Charlottenburg, Abteilung für Neurologie, Freie Universität Berlin, Spandauer Damm 130, D-1000 Berlin 19, Germany **Measurement of diphenylhydantoin and phenobarbital by enzyme immunoassay and gas-liquid chromatography.** *Journal of Neurology (Berlin)*. 213(1):41-46, 1976.

An enzyme multiplied immunoassay technique (EMIT) was compared with gas liquid chromatography (GLC) for the determination of diphenylhydantoin and phenobarbital in plasma. The reproducibility of EMIT and GLC was similar for both drugs and there was good agreement in the results achieved by both techniques. It is concluded that the EMIT system produces accurate and rapid quantitative determinations of diphenylhydantoin and phenobarbital for effective clinical management of epilepsy. 12 references.

001941 Seales, D. M.; Naitoh, P.; Johnson, L. C.; Schuckit, M. no address **The somatosensory evoked potential as a measure of tolerance to alcohol.** *Electroencephalography and Clinical Neurophysiology (Amsterdam)*. 41(6):648, 1976.

At a meeting of the Western EEG Society in San Antonio in February 1976, findings of a study performed to replicate the previously reported alcohol related decrement in somatosensory evoked potential (SEP) recorded from central scalp areas and to determine whether the amount of SEP decrease is related to history of past alcohol use were presented. SEPs, elicited at the vertex by electrical stimulation of the median nerve at the wrist, were significantly reduced by alcohol ingestion compared with placebo. The amount of alcohol induced amplitude reduction correlated significantly with drinking history. Greater amplitude reductions occurred with subjects reporting a lighter drinking history. The SEP appears to be very sensitive to the effects of alcohol on the central nervous system. It is suggested that the SEP may serve as an objective indicator of tolerance to alcohol.

001942 Sjödin, Torgny; Roosdorp, Niek; Sjöholm, Ingvar. Department of Pharmaceutical Biochemistry, Biomedical Center, University of Uppsala, Box 578, S-75123 Uppsala, Sweden **Studies on the binding of benzodiazepines to human serum albumin by circular dichroism measurements.** *Biochemical Pharmacology (Oxford)*. 25(19):2131-2140, 1976.

The binding of 21 different benzodiazepine derivatives to human serum albumin (HSA) is studied by circular dichroism (CD) measurements in 0.1M KCl and 0.005 M phosphate buffer at pH 7.4 and 25 degrees. The data were numerically analyzed with computer programs based on one site, two sites and three sites models. It is concluded that most derivatives will bind primarily to one site on HSA. It is also concluded that variations of the C2 amino side-chains will not influence the binding properties. Oxygens at C2 or C3 will increase the binding while oxygens in both positions will decrease the binding. A derivative with a C7 amino group will show only weak affinity for HSA, which might be explained by the positive character of the hydrogens in the amino group according to the CNDO/2 calculation. A C7 nitro group will also impair the binding, as well as large substituents at N1. 23 references. (Author abstract modified)

001943 Sjölund, Bengt; Eriksson, Margareta. Department of Neurosurgery, Lund University Hospital, S-222 85 Lund,

Sweden **Electro-acupuncture and endogenous morphines.** *Lancet (London)*. No. 7994:1085, 1976.

In a letter to the editor the relationship between the analgesia experienced by patients after a modified electroacupuncture stimulation and the endogenous release of morphine substances is reported. When analgesia had been achieved by electrical stimulation, five patients were given naloxone hydrochloride or saline intravenously in a double-blind procedure. Three of the five patients reported the return of moderate to strong pain when injected with naloxone, whereas the saline injections had no effect. The results suggest that the analgesia produced by an acupuncture like electrical stimulation for the relief of chronic pain is mediated via inhibitory mechanisms releasing endogenous morphine like substances. 10 references.

001944 Smith, Thomas C.; Moyer, Carl E. Parke, Davis and Company, Research Laboratories, Ann Arbor, MI **Bioavailability of two preparations of chlordiazepoxide.** *Current Therapeutic Research*. 20(2):204-210, 1976.

The relative bioavailability of two preparations of the tranquilizer chlordiazepoxide, one available commercially and one a new preparation, was investigated in a crossover study with healthy volunteers. The evaluation was based on comparisons of plasma levels, areas under the plasma drug concentration time curves (AUC), and peak plasma levels attained in the 48 hours after administration of single 20mg doses. The plasma levels, AUC, and peak levels did not differ significantly for the two preparations. Evaluation of the technique of analysis indicated the results obtained were valid. The results of the study indicate the bioavailability of the two preparations of chlordiazepoxide did not differ significantly. 2 references. (Author abstract)

001945 Spirtes, Morris A. General Medical Research, Veterans Administration Hospital, 1601 Perdido Street, New Orleans, LA 70146 **Lithium levels in monkey and human brain after chronic, therapeutic, oral dosage.** *Pharmacology Biochemistry and Behavior*. 5(2):143-147, 1976.

Tissue levels of lithium in 32 brain areas and in most other tissues and organs of macaque rhesus monkeys after chronic administration of lithium carbonate for 3 to 6 weeks were determined. Similar post-mortem studies were carried out in a manic-depressive patient. Lithium levels in two areas of the brain of the human were higher than in the monkeys but lithium levels in a number of the human organs were similar to those in monkeys. Possible conclusions from these values are discussed. 8 references. (Author abstract modified)

001946 Stefanis, Costas N.; Issidorides, Marietta Radovich. Department of Psychiatry, University of Athens, Eginition Hospital, Athens, Greece **Histochemical changes in the blood cells of schizophrenic patients under pimozide treatment.** *Biological Psychiatry*. 11(1):53-68, 1976.

Chromatin structure and nucleohistone pattern were investigated histochemically in the neutrophils of 11 schizophrenics and 16 healthy controls. Compared to controls, all schizophrenic patients prior to medication showed a distinctly different histochemical pattern consisting of increased concentration and abnormal distribution of nucleohistones. This pattern has been attributed to an increase of arginine rich histones in schizophrenics. Pimozide administration exerted a normalizing effect on the nucleohistone distribution pattern. These findings are seen as further support for the view that genomic expression abnormalities may be related to schizophrenic illness. 55 references. (Author abstract)

001947 Sykes, P. A.; Quarrie, J.; Alexander, F. W. Neonatal Unit, Ashington General Hospital, Ashington, Northumberland NE 63 0SA, England **Lithium carbonate and breast-feeding.** *British Medical Journal* (London). No. 6047:1299, 1976.

A case report is studied to gather information on lithium concentrations in human breast milk or in the serum of breastfed infants. Lithium carbonate taken during pregnancy has been associated with neonatal hypotonia and congenital heart disease. The similar serum lithium levels for mother and baby at delivery confirmed that there is free exchange across the placenta. The baby's serum level of lithium fell rapidly in the first week of life. Breast milk lithium levels were about half maternal serum levels and rose with an increase in the oral dose. Despite the rise in concentration achieved in breast milk, the baby's serum levels remained constantly low, much lower than the level to which he had been exposed during pregnancy. Breastfeeding was discouraged and finally stopped at 10 weeks because of the known inhibition by lithium of cyclic 3'5' adenosine monophosphate and the theoretical risk to the developing brain.

001948 Taghavy, A.; Reinhardt, G.; Hermes, K. no address **Effects of ethanol on scalp visual evoked potentials.** *Electroencephalography and Clinical Neurophysiology* (Amsterdam). 41(6):656, 1976.

At a 1975 meeting of the German EEG Society, results of a study on the effects of ethanol on cortical evoked responses to foveal visual stimuli recorded from scalp electrodes were reported. The early components were irregular in their latencies and did not show any consistent changes. The late components showed significant lengthening of latencies of peaks at the height of intoxication. An inverse relationship between peak amplitudes and blood alcohol concentration was revealed. In contrast to the latencies, the amplitudes did not recover fully until the end of the experiments, lasting 6 to 7 hrs.

001949 Verebey, Karl; Volavka, Jan; Mule, Salvatore J.; Resnick, R. B. New York State Office of Drug Abuse Services, Testing and Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Naltrexone: disposition, metabolism, and effects after acute and chronic dosing.** *Clinical Pharmacology and Therapeutics*. 20(3):315-328, 1976.

The disposition of naltrexone during acute and chronic administration of 100mg oral dose was studied in four subjects. Plasma levels of naltrexone and beta-naltrexol measured 24 hr after the daily doses of naltrexone throughout the study indicated that steady state equilibrium was rapidly attained and that there was no accumulation of naltrexone and beta-naltrexol in the plasma after chronic treatment on 100mg oral doses. The renal clearance data indicates that naltrexone is partially reabsorbed while beta-naltrexol is actively secreted by the kidney. During acute and chronic naltrexone administration the mean fecal excretion was 2.1% and 3.6%, while urinary excretion was 38% and 70% of the dose in a 24 hr period. Opiate antagonism to 25mg heroin challenges was nearly complete through 48 hr after naltrexone. At 72 hr the objective responses appeared to a greater extent than the subjective ones. Correlation coefficient (r) between naltrexone plasma levels and opiate antagonism was 0.91, and between individual half-life of naltrexone and opiate antagonism was 0.99. 32 references. (Author abstract modified)

001950 Volavka, Jan; Resnick, Richard B.; Kestenbaum, Richard S.; Freedman, Alfred M. Department of Psychiatry, University of Missouri, 5400 Arsenal St., St Louis, MO **Short-term effects of naltrexone in 155 heroin ex-addicts.** *Biological Psychiatry*. 11(6):679-685, 1976.

In order to find a narcotic antagonist suitable for the maintenance therapy of heroin addicts, the narcotic antagonist naltrexone (N-cyclopropylmethylmorphine hydrochloride) was administered for periods of up to eight months to a total of 155 exaddict patients. The antagonistic effect of naltrexone was tested by injections of heroin. Eighty milligrams of naltrexone was effective for 48 hr. The antagonistic effect decreased at 72 hr after the administration of 120 to 200mg of naltrexone. Laboratory tests indicated no signs of toxicity. Naltrexone may elicit an increase in blood pressure and epigastric pain. Nether of these side-effects appears clinically important. No signs of dependence on naltrexone were detected. These results suggest that naltrexone may be useful for clinical treatment of opiate dependence. 8 references. (Author abstract modified)

001951 Whelpton, R.; Curry, S. H. Department of Pharmacology and Therapeutics, The London Hospital Medical College, Turner Street, London E1 2AD, England **Methods for study of fluphenazine kinetics in man.** *Journal of Pharmacy and Pharmacology* (London). 28(12):869-873, 1976.

An extraction and identification method for fluphenazine and its principal metabolites, fluphenazine sulfoxide and 7-hydroxyfluphenazine, following intramuscular (IM) and oral administration of fluphenazine is described. Plasma, urine, and feces were collected from patients receiving fluphenazine, and fluphenazine and its principal metabolites, as well as a conjugate fraction, were identified and measured. Injection of fluphenazine di-HCl resulted in a peak plasma concentration at 2 h and a half-life of 15 h. In the urine, the metabolites were mainly conjugated, but no conjugates were found in the feces. The 24 h urinary excretion was measured in a patient receiving 50mg fluphenazine decanoate at weekly intervals. 17 references.

001952 Wirz-Justice, Anna; Chappuis-Arndt, Elfriede. Psychiatrische Universitätsklinik Basel, Wilhelm Kleinstrasse 27, CH-4025 Basel, Switzerland. **Sex specific differences in chlorimipramine inhibition of serotonin uptake in human platelets.** *European Journal of Pharmacology* (Amsterdam). 40(1):21-25, 1976.

Sex specific differences in chlorimipramine inhibition of serotonin uptake in human platelets were studied. The uptake of C-14 5-hydroxytryptamine (5-HT) was measured in a scintillation counter after incubation of platelet rich plasma of clinically healthy men and women. 5-HT uptake was similar in men and women, but the uptake inhibition by chlorimipramine was significantly less in women than in men. The extent of this inhibition could be correlated with the stage of the menstrual cycle which did not affect the uptake of 5-HT alone. The results suggest the modifying influence of hormonal factors and may indicate an endogenous hormonal modulation of 5-HT uptake across the platelet membrane or possible differences in the plasma protein binding of chlorimipramine. 18 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

001953 Agnoli, A.; Andreoli, V.; Casacchia, M.; Cerbo, R. Clinica delle Malattie Nervose e Mentali, Università di Roma, Roma, Italy **Effect of S-adenosyl-L-methionine (SAME) upon depressive symptoms.** *Journal of Psychiatric Research* (Oxford). 13(1):43-54, 1976.

A double-blind trial was carried out in 30 patients (20 were treated with S-adenosyl-L-methionine (SAME) and 10 received a placebo) who were then given the Hamilton Depression Rat-

ing Scale in a study of the effects of SAME upon depressive symptoms. The drug appeared to have a rapid and beneficial effect mainly upon depressed mood, suicidal tendencies, retardation, and performance. Improvement was observed in 80% of the cases in 4 days to 6 days. No untoward side-effects were observed in the patients receiving SAME. 5 references.

001954 Alkana, R. L.; Parker, E. S.; Cohen, H. B.; Birch, H.; Noble, E. P. Pharmaceutical Science Center, School of Pharmacy, University of Southern California, 1985 Zonal Avenue, Los Angeles, CA 90033 **Reversal of ethanol intoxication in humans: an assessment of the efficacy of propranolol.** *Psychopharmacology (Berlin)*. 51(1):29-37, 1976.

The effect on acute intoxication of postethanol ingestion of a single dose of propranolol was studied in 13 healthy male volunteer subjects. Ethanol significantly reduced motor coordination, memory and divided attention performance, and altered mood scores. Propranolol significantly increased ethanol's effects on divided attention, inebriation ratings, and the electroencephalogram without significantly altering blood alcohol concentrations. In contrast to previous investigations in which pretreatment with propranolol attenuated acute effects of ethanol in animals and in humans, there was no indication that postethanol administration of propranolol antagonized any of the effects of ethanol. These results agree with studies indicating that the effects of ethanol are increased by a reduction in the functional capacity of central catecholamine systems. It is suggested that central catecholamine stimulating drugs may reverse some of ethanol's effects. 52 references. (Author abstract modified)

001955 Angrist, Burton; Thompson, Hyacinth; Shopsin, Baron; Gershon, Samuel. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York University Medical Center, 550 1st Street, New York, NY 10016 **Clinical studies with dopamine receptor stimulations.** *Journal of Psychiatric Research (Oxford)*. 13(1):60, 1976.

In a summary of a paper read before the Psychiatric Research Society, New York, October 31 to November 1, 1975, oral administration of ET-495 (a dopamine agonist) was found to cause deterioration of psychiatric state in four out of seven schizophrenic patients, and to induce a paranoid state and a syndrome of auditory hallucinosis in two nonschizophrenics. These observations were compatible with the hypothesized role of dopamine in schizophrenia. However, these psychotogenic effects were far less dramatic than those noted in other studies with amphetamine, methylphenidate or L-dihydroxyphenylalanine (L-Dopa). Possible explanations for this differing psychotogenic potency of receptor stimulators vs presynaptic agonists are presented. Intravenous ET-495 and apomorphine did not show psychotogenic effects. (Journal abstract)

001956 Appel, Philip W.; Gordon, Norman B. New York State Office of Drug Abuse Services, 2 World Trade Center, New York, NY 10047 **Digit-symbol performance in methadone-treated ex-heroin addicts.** *American Journal of Psychiatry*. 133(11):1337-1339, 1976.

The digit symbol substitution task (DSST) of the Wechsler Adult Intelligence Scale was given to working and nonworking (MNV) patients on high dose methadone maintenance and to two comparison groups to assess the function of attention in these patients. Mean DSST scores were significantly lower for the MNV group than for the other three groups, which did not differ. However, the scores for the MNV group were within the normal range. DSST scores and length of methadone treat-

ment (range: 11 months to 8 years) were positively correlated, providing no evidence of deterioration with increasing duration of treatment. 13 references. (Journal abstract)

001957 Baust, W. Neurologische Klinik der Universität Dusseldorf, Moorenstrasse 5, D-4000 Dusseldorf 1, Germany **Sleep and psychotropic drugs: clinical aspects.** *Schlaf und Psychopharmaka: Klinische Aspekte. Arzneimittel-Forschung (Aulendorf)*. 26(6):1039-1041, 1976.

The effects of psychotropic drugs on sleep are discussed. Subjects with sleep disturbances cannot accurately rate the effectiveness of hypnotics. As an illustration of this point, a group of subjects were asked to estimate how long it took them to fall asleep. The subjects gave an average estimate of 59 minutes; actually, it took them only 15 minutes to fall asleep as measured by the investigators. All psychotropic drugs with hypnotic effects reduce stage 4 sleep and REM sleep. Barbiturates caused a massive reduction of stage 4 sleep and a reduction in REM sleep; after discontinuation of the barbiturate, there was a rebound effect in REM sleep. Glutethimide and methypyrion caused a massive rebound in both stage 4 sleep and REM sleep. Methaqualone reduced REM sleep only when given in large doses. Chloral hydrate did not significantly change the physiological sleep profile. Chlor-diazepoxide and diazepam do not alter REM sleep, but reduce stage 4 sleep. The tricyclic antidepressants increase deep sleep, but reduce REM sleep. Clozapine increases REM sleep up to 85% of total sleep time, whereas chlorpromazine and reserpine cause only a slight increase in REM sleep. Sleep changes in schizophrenia, alcoholic states, and depression are briefly considered.

001958 Belyakova, L. I. no address **Action of psycholeptics on some physiological indices in stutterers.** *Osobennosti deystviya psikholeptikov na nekotoryye fiziologicheskiye pokazateli u bol'nykh s zaikaniem. Zhurnal Nevropatologii i Psikiatrii imeni S.S. Korsakova (Moskva)*. 76(9):1386-1391, 1976.

Effects of single doses of aminazine, seduxen, and benzacetyline on various physiological indicators during rest and during the process of speech in 25 individuals with stuttering or neurotic disturbances and in 20 cases of early organic lesions were investigated. Drug action was evaluated by effects on the EMG of the orbicular muscle of the mouth, pulse frequency, GSR, and EEG. It is concluded that there is a selective effect of these drugs on the different structures of the functional brain system in stutterers. 11 references. (Author abstract modified)

001959 Blau, Sheldon P.; Blau, Bette. State University of New York Stony Brook, NY **Sex and systemic lupus erythematosus.** *Medical Aspects of Human Sexuality*. 10(11):93-94, 1976.

A brief consideration of symptoms affecting libido in patients with systemic lupus erythematosus is presented with a description of drugs used for treatment of lupus which can improve a couple's sexual relationship. Symptoms affecting libido include: 1) vaginal ulcers; 2) mouth ulcers; 3) Sjogren's syndrome; and 4) Raynaud's phenomenon. Drug effects on libido include: 1) orgasm suppression with tranquilizers; 2) impotence with antihypertensives; 3) libidinal effects of immunosuppressives; and 4) skin bruising, amenorrhea, avascular necrosis, and sexual apathy with cortisone.

001960 Boucsein, W. Fachbereich 2, Fach Psychologie der Gesamthochschule Duisburg, Lotharstrasse 65, D-4100 Duisburg, Germany **Experimental psychological study of the ef-**

fect of tranquilizers (diazepam and a test drug) on personality traits./ Experimentalpsychologische Untersuchung zur Wirkung von Tranquilizern (Diazepam und einer Prüfsubstanz) unter Berücksichtigung von Persönlichkeitsmerkmalen. Arzneimittel-Forschung (Aulendorf). 26(6):1138-1141, 1976.

Bay-g-5653, a thienodiazepine under investigation, was compared with diazepam, placebo, and no medication in 180 male student volunteers. Bay-g-5653 was given in doses of 2.5, 5, and 10mg, compared to 5mg diazepam. The procedure was double-blind. White noise of 95db was the employed factor. The emotionally stable subjects (as measured by the Freiburger Personality Inventory) showed less activation under diazepam and 10mg Bay-g-5653 during the white noise than with placebo, and an increase in general well-being under 2.5 to 5mg Bay-g-5653. The emotionally labile subjects showed an improvement in general well-being only under diazepam. On the Adjective Word List, subjects receiving BY g 5653 and diazepam showed less activation, and subjects receiving Bay-g-5653 showed less anxiety than subjects on placebo. Emotionally labile subjects receiving Bay-g-5653 showed a greater increase in general activity on the Adjective Word List than labile subjects receiving diazepam. The latter showed significantly less general activity than emotionally stable subjects receiving diazepam. Labile subjects receiving 2.5 to 5mg Bay-g-5653 showed more extroversion on the Adjective Word List than labile subjects receiving placebo or diazepam, and stable subjects showed more extroversion than labile subjects on diazepam. 8 references.

001961 Boxer, Candida M.; Herzberg, J. L.; Scott, D. F. EEG Department, Section of Neurological Sciences, The London Hospital, London, England Has sodium valproate hypnotic effects? *Epilepsia*. 17(4):367-370, 1976.

A study is conducted to determine whether sodium valproate has hypnotic effects. Eight fasting normal subjects were given a single dose of sodium valproate, 400 mg, phenobarbital, 60 mg, or the two drugs in combination, in a double-blind placebo controlled study. The effects were assessed behaviorally and by a standard 30 min EEG begun one hour after the treatments had been given. The recording was rated for the amount of drowsiness and sleep, independent of which drug had been given. The scores obtained indicated that valproate itself had hypnotic action and a tendency to increase effectiveness by the simultaneous administration of phenobarbital. 7 references. (Author abstract modified)

001962 Bunney, William E., Jr.; Post, Robert M. Adult Psychiatry Branch, DCBR, National Institute of Mental Health, Bethesda, MD 20014 Catecholamine agonist and receptor hypothesis of affective illness (paradoxical drug effects). (Unpublished paper). Washington, DC, NIMH, 1976.

Some of the behavioral effects of pharmacological agents are reviewed which are incompatible with the catecholamine hypothesis that depression is a result of decreased norepinephrine (NE) and/or dopamine (DA) brain levels and that mania results from increased levels of NE and/or DA in the brain. Data suggesting that one drug can produce opposite behavioral effects in apparently identical psychopathological states are discussed. Specific drugs discussed are: lithium, dihydroxyphenylalanine (DOPA), cocaine, the phenothragines and butyrophenones, and reserpine in depression; and alpha-methyl-para-tyrosine (AMPT) and pibedil (ET-495) in mania. Hypothetical models of neuronal receptor sensitivity in affective illness are presented. A mechanism by which the effects of some psychoactive drugs might be amplified by alterations in neuronal receptor sensitivity is suggested. 29 references.

001963 Butler, John L.; Gaines, Lawrence S.; Lenox, John R. St. Clare's Hospital, Denville, NJ Effects of marihuana, expectation and "suggestibility" on cognitive functioning. *Perceptual and Motor Skills*. 42(3):1059-1065, 1976.

The influence of socially provided information about some of marihuana's physiological effects on cognitive tasks is examined for subjects differing in suggestibility proneness. It was predicted that: 1) highly suggestible subjects, when told they would be smoking high dose marihuana, would perform cognition tasks less well than similar subjects given no dosage information; and 2) that for socially suggestible subjects the activation of marihuana associated relationships would be more efficient. The results indicate a significant postmarihuana deficit on some tasks not The results indicate a significant postmarihuana deficit on some tasks not sensitive to effects of suggestibility or information. 22 references.

001964 Chatwin, J. C.; Johns, W. L. Medical Arts Clinic, Regina, Saskatchewan, Canada Triazolam: an effective hypnotic in general practice. *Current Therapeutic Research*. 21(2):207-214, 1977.

An open label study of triazolam, a new benzodiazepine derivative, was conducted in a group of 30 private practice patients to determine its tolerance and hypnotic properties when used at two different dose levels. Patients were prescribed 0.25mg. of triazolam to be taken at bedtime for two consecutive nights, with an option to increase the dose to 0.5mg. on the third through the seventh night if insufficient hypnotic effect had been obtained at the lower dose. Of the 28 patients who completed the study, 8 required an increase of the dose to the 0.5mg. level. Side effects were reported by only 4 of the patients and, in each instance, were considered mild. Most patients expressed satisfaction with triazolam. 7 references. (Author abstract modified)

001965 Davis, Kenneth L.; Hollister, Leo E.; Overall, John; Johnson, Anne; Train, Karen. Departments of Medicine and Psychiatry, Stanford University, Stanford, CA Physostigmine: effects on cognition and affect in normal subjects. *Psychopharmacology (Berlin)*. 51(1):23-27, 1976.

The effects of intravenous administration of physostigmine on memory and on affective state were studied in 23 normal volunteer subjects. A physostigmine syndrome consisting of decreased speech, slowed thoughts, mild sedation, expressionless faces, nausea and decreased spontaneous activity occurred following drug administration. Two of 13 subjects became tearful and depressed. The capacity of short-term memory (STM) as measured by digit span tasks was significantly less for physostigmine treated subjects than for controls. No difference was observed between the two groups on tasks of consolidation from STM to long-term memory. 18 references. (Author abstract modified)

001966 Dickerson, Lawrence L.; Ferraro, Douglas Peter. Department of Psychology, University of New Mexico, Albuquerque, NM 87131 Effects of alcohol on specific and environmental fear. *Psychological Reports*. 39(3, part 2):1335-1342, 1976.

To assess the effects of alcohol on specific and environmental fear, 64 rats were exposed to a conditioned emotional response situation in which a stimulus warned of the imminent delivery of shock. Alcohol retarded the acquisition of fear to environmental stimuli much more than to a specific warning stimulus. The effects of alcohol on environmental fear were transitory, with no transfer of alcohol induced reduction of

fear to the nondrug state. Results are discussed in terms of: 1) the possible adaptive function of alcohol for the normal person; and 2) a potential method of identifying persons prone to become pathological drinkers. 15 references. (Author abstract modified)

001967 Dimond, Stuart J.; Brouwers, E. Y. M. Dept. of Psychology, University College, P. O. Box 78, Cardiff CF1 1XB, Wales, England **Increase in the power of human memory in normal man through the use of drugs.** *Psychopharmacology* (Berlin). 49(3):307-309, 1976.

Nootropyl (Piracetam) a drug reported to facilitate learning in animals was tested for its effect on man by administering it to normal volunteers. The subjects were given 3 x 4 capsules at 400mg per day in a double-blind study. Each subject learned series of words presented as stimuli upon a memory drum. No effects were observed after 14 days verbal learning had significantly increased. 10 references. (Author abstract)

001968 Firmau, G.; Garnett, E. S.; Chan, P. K. H.; Belbeck, L. W. McMaster University Medical Centre, Department of Nuclear Medicine, Hamilton, Ontario, Canada **Intracerebral dopamine metabolism studied by a novel radioisotope technique.** *Journal of Pharmacy and Pharmacology* (London). 28(7):584-585, 1976.

Results are reported for research that (18F)fluoro-dopa is a radioactive analogue of dopa which can be injected intravenously and used to study intracerebral dopamine metabolism in man by means of routine noninvasive isotopic procedures. Experiments with rats and mice established the biochemical and biological properties of fluorodopa, and research with a conscious female baboon showed the ability of reserpine, known to reduce dopamine accumulation in the brain, to detect changes in the amount of 18F present in the head after an intravenous injection of the fluorodopa. Implications of results are that fluorodopa can be used to study intracerebral dopamine metabolism in man, as well as in other primates, provided that it is proved that addition of fluorine to the dopa molecule does not produce any untoward toxic effects. It is suggested that a protocol similar to that used in the baboon experiments could be used to study the role of dopamine in disorders of locomotion and affect/mood, as well as the pharmacology of the wide variety of psychotropic drugs presently marketed. 8 references.

001969 Gaillard, Jean-Michel; Phelippeau, Marc. Clinique Psychiatrique, Université de Genève, Bel-Air, CH-1225 Chêne-Bourg, Switzerland **Benzodiazepine-induced modifications of dream content: the effect of flunitrazepam.** *Neuropsychobiology* (Basel). 2(1):37-44, 1976.

The effect of the hypnotic flunitrazepam on dream content was studied in 8 normal volunteers. The subjects were usually good sleepers and very rarely experienced unpleasant dreams. Each subject spent seven nights in the laboratory: one habituation night, three placebo nights, and three drug nights. Subjects were awakened during REM sleep and in stage 2 sleep, and their dream content was scored for unreality, participation of the dreamer, pleasantness, unpleasantness, verbal aggressivity, physical aggressivity, sexuality, sensoriality, and time of reference in the dreamer's life. Subjects experienced more very unpleasant dreams under flunitrazepam than under placebo. The dream content under the drug was higher in unpleasantness, verbal aggressivity, physical aggressivity, and sexuality, which was related to a disinhibitory effect of the drug. 22 references. (Author abstract modified)

001970 Janowsky, David S. Dept. of Psychiatry, University of California at San Diego, School of Medicine, La Jolla, CA 92037 **Neurotransmitter and psychostimulant induced psychosis activation.** *Journal of Psychiatric Research* (Oxford). 13(1):59-60, 1976.

In a summary of a paper read before the Psychiatric Research Society, New York, October 31 to November 1, 1975, experiments which use psychostimulants and cholinomimetics as research tools to explore the phenomena of psychostimulant induced psychosis activation are related to the schizophrenic process. Psychostimulants, including D-amphetamine, L-amphetamine, and methylphenidate have been shown to selectively intensify psychotic symptoms in acutely ill schizophrenic patients. It has been shown that low doses of methylphenidate significantly increase the number of pathologic Holtzman ink blot responses in acutely ill inpatient schizophrenics, but not in nonpsychotic inpatients; and that methylphenidate also causes a decrease in the commonality of word associations in actively ill schizophrenics, but not in nonpsychotics. This suggests that psychostimulant induced psychosis activation effects the basic or primary schizophrenic process, rather than merely increasing trust, interactions, and talkativeness, or effecting secondary schizophrenic symptoms such as delusions or hallucinations. Such an effect appears to be relatively specific to schizophrenic patients. Psychopharmacologic information which demonstrates that dopamine may be involved in the activation of schizophrenic symptoms is reviewed, and it is suggested that psychotic symptom activation and inhibition may be based on a circuitry involving at least three neurotransmitters. (Journal abstract modified)

001971 Jinks, Martin. Dept. of Professional Services, Health Application System, Burlingame, CA 94010 **Insomnia and its treatment.** *Journal of the American Pharmaceutical Association*. 16(11):613-616, 1976.

The different types of insomnia and sleep disorders, the methods of evaluating hypnotic drug efficacy, and the relation of rapid eye movement (REM) and nonREM (NREM) sleep to insomnia are reviewed. The presumed differences between hypnotics and nonhypnotics in terms of pharmacologic properties, physiologic effects in humans, and effects on REM and NREM sleep are discussed. The properties of the barbiturates (pentobarbital, secobarbital), the glutarimides (glutethimide and methyprylon) and methaqualone, halogenated hydrocarbons (chloral hydrate, ethchlorvynol), the benzodiazepines (flurazepam), and the tricyclic antidepressants are detailed with note of their therapeutic advantages and disadvantages. Eight therapeutic guidelines for the use of hypnotic drugs are given and a protocol for discontinuance of hypnotic drugs with minimal withdrawal symptoms is suggested. 19 references.

001972 Kales, Anthony; Hauri, Peter; Bixler, Edward O.; Silberfarb, Peter. Sleep Research and Treatment Center, Milton S. Hershey Medical Center, Hershey, PA 17033 **Effectiveness of intermediate-term use of secobarbital.** *Clinical Pharmacology and Therapeutics*. 20(5):541-545, 1976.

Secobarbital was evaluated in two separate sleep laboratory drug evaluation studies, each with 4 insomniac patients. In both studies, the effect of secobarbital in inducing and maintaining sleep was evaluated, as well as the effects of the drug on sleep stages. Statistical analysis demonstrated that the results of the two studies could be combined. With short-term drug administration of secobarbital (up to 3 nights), there was an improvement in both sleep induction and sleep maintenance. Total wake time was decreased 43% below baseline and was consistently decreased in each third of the night. With

intermediate term drug administration, total wake time was decreased only 14% (not statistically significant). Following drug withdrawal, the degree of sleep difficulty returned to baseline levels. The results indicate that secobarbital 100mg is effective for short term use, but loses much of its effectiveness with intermediate use, suggesting that the drug is of limited value for insomniac patients who require nightly medication beyond a short period. With short-term administration, secobarbital induced a slight decrease in rapid eye movement (REM) and slow-wave sleep and a significant increase in stage 2 sleep. With intermediate administration, sleep stage values were similar to baseline levels. Following withdrawal, there was only a minimal increase in REM sleep above baseline levels, a significant increase in stage 3 sleep, and a significant decrease in stage 2 sleep. The rebound increase in stage 3 is similar to that reported following withdrawal of pentobarbital. 12 references. (Author abstract modified)

001973 Karacan, Ismet; Thornby, John I.; Anch, Michael A.; Booth, Glenn H.; Williams, Robert L.; Salis, Patricia J. Sleep Disorders Center, Department of Psychiatry, Baylor College of Medicine, Houston, TX **Dose-related sleep disturbances induced by coffee and caffeine.** *Clinical Pharmacology and Therapeutics.* 20(6):682-689, 1976.

The effects of various doses of caffeine, administered 30 min before bedtime as regular coffee or as the chemical, on sleep were examined in 18 healthy adult males over a 13 night period. Regular coffee produced dose related changes in most standard electroencephalogram and electrooculogram sleep parameters; equivalent doses of caffeine as regular coffee and as chemical caffeine produced equivalent effects. Decaffeinated coffee had no effect. Regular coffee and caffeine caused rapid eye movement sleep to shift to the early part of the night and stages 3 and 4 sleep to shift to the later part. Coffee also produced dose related changes in several subjective estimates of sleep characteristics. It is suggested that coffee and caffeine may be used in normal subjects to induce symptoms mimicking those of insomnia to promote further understanding of insomnia. 26 references. (Author abstract modified)

001974 Karniol, Isaac G.; Dalton, J.; Lader, Malcolm. no address **Comparative psychotropic effects of trazodone, imipramine and diazepam in normal subjects.** *Current Therapeutic Research.* 29(3):337-348, 1976.

The psychological effects and physiological effects of trazodone were compared with those of imipramine, diazepam, and placebo in a double-blind study in healthy subjects. Compared to placebo, trazodone produced subjective feelings of impairment and decrement in motor performance. Trazodone increased the percentages of slow waves, total voltage of the EEG, and the amplitude of the EEG evoked response. Trazodone decreased skin conductance (sweating), the percentage of fast waves in the EEG, the peak frequency of finger tremor, the pupil size, and the diastolic blood pressure. Diazepam was no different from placebo in most tests but any effects which did occur were opposite to those of trazodone. Although some central effects of imipramine resembled those of trazodone, imipramine produced less subjective impairment than trazodone. In other tests, the physiological effects of imipramine were different than those of trazodone. It is concluded that the profile of action of trazodone in normal subjects is atypical of anxiolytic drugs and antidepressant drugs. 17 references. (Author abstract modified)

001975 Koella, W. P. Biologische Forschungsabteilung, Ciba-Geigy AG, CH-4002 Basel, Switzerland **Introduction: importance of psychotropic drugs in sleep research./ Einleitung: Bedeutung der Psychopharmaka im Rahmen der Schlaf-forschung.** *Arzneimittel-Forschung (Aulendorf).* 26(6):1030-1031, 1976.

Studies of the effect of psychotropic drugs on sleep are considered in general. The rationale for investigating the effects of psychotropic drugs on sleep is that sleep is a normal phenomenon, dreams are related to hallucinations and psychosis, and sleep disturbances occur in practically every psychiatric disturbance. Animal sleep has much in common with human sleep. Sleep in humans into 5 phases: 20 to 25% REM sleep, 50 to 55% stage 2 sleep, 20% stages 3 and 4 sleep, and about 5% stage 1 sleep.

001976 Koella, W. P. Biologische Forschungsabteilung, Ciba-Geigy AG, CH 4002 Basel, Switzerland **Summary on psychopharmacology in sleep research./ Epilog.** *Arzneimittel-Forschung (Aulendorf).* 26(6):1047-1049, 1976.

Sleep research and pharmacopsychiatry are discussed. The subjects of psychotropic drugs, sleep, and mental illness can be represented as the apices of a triangle, with each side representing a relationship between variables. REM rebound can occur following amphetamines, barbiturates, and tricyclic drugs. Different psychiatric illnesses can accompany sleep disorders, and sleep disturbances can appear as the first symptom of a mental illness. In depression, sleep is fragmented and light, with an increase in stage 1 sleep and a decrease of stages 3 and 4 and REM sleep. In schizophrenia, there is a decrease of stage 3-4 sleep, whereas in anxiety, there is increased latency of sleep. Sleep is affected by the neurotransmitters serotonin, acetylcholine, dopamine, and norepinephrine. The effect of psychotropic drugs on these neurotransmitters and the possible relationships of these neurotransmitters to mental illnesses are briefly reviewed. 40 references.

001977 Lehmann, E. Psychologisches Institut, Universität Dusseldorf, Chlodwigstrasse 80, D-4000 Dusseldorf, Germany **Internal and external stress, tybamate, and secobarbital: an experimental investigation of their interaction./ Innerer und ausserer Stress, Tybamate und Secobarbital: eine experimentelle Untersuchung ihrer Interaktion.** *Arzneimittel-Forschung (Aulendorf).* 26(6):1132-1133, 1976.

The hypothesis that barbiturate reduces external stress while tranquilizers reduce internal (i.e. ego involved) stress was tested in a double-blind experiment. Preparations administered were: placebo; 500mg tybamate; 100mg secobarbital. Stress conditions were: white noise of 95 db as external stress, a negative opinion as the internal stress, and no stress as the neutral condition. Subjects were 117 healthy male students with average scores on a neuroticism questionnaire. Subjects rated themselves on a 72 item list which measured activation, deactivation, fatigue, carefreeness, adjustment, mood, excitation, depression or discouragement, anxiety, and anger. Physiological measurements were made of blood pressure, pulse, respiration rate, and galvanic skin response (GSR). Both stresses increased the physiological measurements. Secobarbital and tybamate both lowered blood pressure and GSR, but increased respiration rate. Secobarbital reduced excitation, while tybamate increased excitation and anger. The interaction between barbiturates and external stress, and tranquilizers and internal stress was not demonstrated. 5 references.

001978 Loew, D. M.; Spiegel, R. Biological and Medical Research Division, Sandoz, Ltd., CH-4002 Basel, Switzerland

Polygraphic sleep studies in rats and humans: their use in psychopharmacological research. *Arzneimittel-Forschung* (Aulendorf). 26(6):1032-1035, 1976.

The effect of centrally acting drugs on sleep in rats and humans was studied. The drugs studied were d-amphetamine, nitrazepam, mesoridazine, imipramine, and bromocriptin, a central dopamine agonist. The animals were male Wistar rats weighing 450-550g, bearing chronically implanted EEG and EMG electrodes. Recordings were made between 10 a.m. and 4 p.m. on 3 consecutive days, with placebo given i.p. the 1st and 3rd days and the drug given i.p. the 2nd day. Normal male volunteers between 20 and 30 years old were studied on 4 to 5 consecutive nights. Treatments were arranged in a square design and sleep was recorded between 10:30 p.m. and 6 a.m. Amphetamine reduced total sleep time and both NREM and REM sleep in rat and human. Nitrazepam had little effect on sleep in humans. Mesoridazine had a sedative effect in both rat and human; however, at the highest dose, total sleep time was reduced in the rat and REM sleep was virtually absent. Imipramine caused a dose dependent reduction in REM sleep in both species. Stage 1 sleep was prolonged in humans and wakefulness was prolonged in rats. Bromocriptin increased total sleep time in rats and had no pronounced effects in humans. The 5 different drug classes can thus be differentiated by their effects on sleep stages in rats and humans. Investigations in normal subjects and animals appear to be relevant for the study of CNS stimulants, whereas for CNS depressants, studies in sleep disturbed subjects and animals appear to be more dependable. 26 references.

001979 Malek-Ahmadi, Parviz; Behrmann, Paul J. Department of Psychiatry, University of Missouri, Columbia, MO 65201 **Depressive syndrome induced by oral contraceptives.** *Diseases of the Nervous System*. 37(7):406-408, 1976.

The biochemical and psychological aspects of the depressive syndrome induced by oral contraceptives are reviewed, and guidelines are recommended for recognition and management of the problem. It has been demonstrated that a small proportion of women taking oral contraceptives develop a depressive syndrome characterized by despondency, tension and changes in sex desire. Although disturbed tryptophan metabolism induced by estrogen has been held responsible for this syndrome, the role of psychological factors should not be overlooked. Recognition and management of the syndrome require information concerning the pharmacological actions of the oral contraceptives and the personality makeup of the patient. 20 references. (Author abstract)

001980 Melges, Frederick Towne. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Tracking difficulties and paranoid ideation during hashish and alcohol intoxication.** *American Journal of Psychiatry*. 133(9):1024-1028, 1976.

In a double-blind study using six normal subjects each under his own control, 20mg of THC was smoked within 10 and 45 minute periods (fast and slow conditions respectively) to review the occurrence of persecutory ideation when difficulties with tracking information over time disrupt ongoing self/other metaperspectives. Each subject also received placebo and doses of alcohol calculated to be as intoxicating as the THC doses. In fast conditions, THC induced greater difficulties with tracking information over time, greater disruptions of self/other interpersonal perceptions, and more persecutory ideation than did alcohol or placebo. Similar but less marked differences were found in the slow conditions. As hypothesized, changes in tracking difficulties, self/other

metaperspectives, and persecutory ideation were substantially and significantly correlated. 10 references. (Journal abstract modified)

001981 Mendelson, Jack H. Harvard Medical School, Boston, MA **Marihuana and sex.** *Medical Aspects of Human Sexuality*. 10(11):23-24, 1976.

Counseling patients about the effects of marihuana and sex is briefly discussed with reference to current experimental findings and physician's responsibility. It is noted that: 1) marihuana itself does not affect sexual function; 2) studies on experimental animals cannot be applied to humans; and 3) changes in male plasma testosterone levels are not biologically significant. The therapist is advised not to reinforce or challenge a patient's personal beliefs regarding drug use and sex.

001982 Naliboff, Bruce D.; Rickles, William H.; Cohen, Michael J.; Naimark, Robert S. Department of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Interactions of marijuana and induced stress: forearm blood flow, heart rate, and skin conductance.** *Psychophysiology*. 13(6):517-522, 1976.

To examine the interaction of marijuana and an induced state of stress, on both subjective and physiological measures, two groups of 15 subjects each were given a mental arithmetic task to perform. The sequence of events was 10 min each of prestress, stress, poststress, intoxication (about 20 min), prestress, stress, poststress. In the intoxication phase, one group smoked marijuana containing 14mg delta9-THC while the other group smoked a placebo. The dependent variables were forearm blood flow (FBF), heart rate (HR), and skin conductance, and a subjective measure of stress - the Multiple Affect Adjective Checklist. The results revealed all physiological variables to be reactive to the stress task. In addition, marijuana intoxication produced reliable increases in both prestress HR and FBF, and yet the physiological response to the postintoxication stress period showed no significant decrement when compared to the placebo group. Discussion of these results centered around marijuana's effects on tonic and phasic reactivity. 27 references. (Author abstract)

001983 Pacifici, G. M. no address **Amantidine reduces drug-induced parkinsonism.** *British Journal of Clinical Pharmacology* (London). No. 3:883, 1976.

The effects of amantidine on the drug induced Parkinsonian extrapyramidal syndrome were investigated in 15 female psychiatric patients in a double-blind crossover study. All patients were on neuroleptics and anticholinergic drugs, but their extrapyramidal symptoms were poorly controlled. While the usual neuroleptics were continued, the anticholinergics were replaced by amantidine in a dose of 200mg/day or placebo for 15 days. Findings indicate that amantidine antagonized the extrapyramidal symptoms within 4 to 6 days, and that steady state levels were reached in 4 to 7 days at individual plasma levels of 200 to 900micrograms/ml. There was a significant relationship between mean amantidine plasma levels and the effects on extrapyramidal side-effects. Data suggest a direct effect of amantidine on the dopaminergic receptors. (Journal abstract modified)

001984 Polivy, Janet; Schueneman, Arthur L.; Carlson, Kathleen. Department of Psychology, Loyola University, Chicago, IL 60626 **Alcohol and tension reduction: cognitive and physiological effects.** *Journal of Abnormal Psychology*. 85(6):595-600, 1976.

The effect of cognitive and social variables on the tension reduction associated with alcohol ingestion was studied in 40 undergraduates through manipulating subjects' expectancies. Although alcohol reduced tension more than a placebo, the cognition that alcohol was being ingested increased anxiety as measured by changes in heartrate, electromyographic activity, and electroencephalographic activity. The strong anxiety producing effect found in being told one is drinking alcohol may be a function of the setting and the subjects' lack of experience with alcohol. It is suggested that the tension reducing effects of alcohol may be overridden by prior negative experiences or lack of prior positive experiences. 15 references. (Author abstract modified)

001985 Priest, R. G.; Rizvi, Z. A. St. Mary's Hospital Medical School, London, England Nitrazepam and temazepam: a comparative trial of two hypnotics. *Journal of International Medical Research* (Northampton). 4(3):145-151, 1976.

The performance of two hypnotic drugs, nitrazepam and temazepam, was evaluated using a specially designed sleep questionnaire. Psychiatric patients were given 5mg nitrazepam or 10mg temazepam in identical capsules and were given more on demand. A double-blind crossover design was used to eliminate observer bias as an intervening variable. The two regimes showed few differences, and produced fairly similar reports on patient satisfaction, quality of sleep, number of awakenings, depth of sleep and other variables. Patients on nitrazepam were a little more clear headed in the morning, though they tended to wake later, sleep longer, and take more sleep over the 24 hour period. No toxicity was found with either drug over the 434 patient days of administration. In view of the advantages of the benzodiazepine drugs over their predecessors, the further study of temazepam as a sleep inducing drug is encouraged. 10 references.

001986 Raskin, Allen; Crook, Thomas H. Psychopharmacology Research Branch, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20852 Sensitivity of rating scales completed by psychiatrists, nurses and patients to antidepressant drug effects. *Journal of Psychiatric Research* (Oxford). 13(1):31-41, 1976.

The comparative sensitivity to antidepressant drug effects of rating scales completed by psychiatrists, nurses, and patients were examined in two multihospital collaborative drug trials. There were 555 patients in the first study where the treatments were chlorpromazine (Thorazine), imipramine (Tofranil), and a placebo; and there were 325 patients in the second study where the treatments were diazepam (Valium), phenelzine (Nardil), or a placebo. The eight evaluation instruments common to both studies showed considerable variability in detecting significant drug effects. The Inventory of Psychic and Somatic Complaints (IPSC) was a more sensitive instrument in the hands of the psychiatrist than when completed by patients, whereas the National Institute of Mental Health Mood Scale (MS) uncovered more significant drug effects when completed by patients than when completed by the study nurse. The Brief Psychiatric Rating Scale (BPRS) and the Inpatient Multidimensional Psychiatric Scale (IMPS) showed less sensitivity to antidepressant drug effects than the IPSC. The Ward Behavior Rating Scale and the Global Behavior Scales completed by nurses proved to be most helpful for detecting the sedative hypnotic effects of the study drugs. 22 references.

001987 Richter, R.; Hobi, V. Psychiatrische Universitätsklinik Basel, Wilhelm-Klein-Strasse 27, CH-4025 Basel, Switzerland /Personality specific effect of a tranquilizer./ Die persönlichkeitspezifische Wirkung eines Tranquilizers. *Arzneimittel-Forschung* (Aulendorf). 26(6):1136-1138, 1976.

Bromazepam, a benzodiazepine derivative, was compared with placebo in 45 students with average age 22 years. Students selected had more than one standard deviation on the emotional lability scale of the Freiburger Personality Inventory. The emotionally labile and emotionally stable groups were randomly divided in half and given 1.5mg bromazepam or placebo. Bromazepam had no significant effect on vitality or excitation. On the tapping test, the tempo was higher in subjects receiving placebo than in those receiving bromazepam. In the line tracing test, the length of contact was significantly reduced in the bromazepam groups. In the attention test, performance was decreased by the drug in the stable group, but had no effect in the labile group. The drug had no effect in the tracking test. Critical flicker fusion and afterimage of spiral rotor were also unaffected by the drug. 12 references.

001988 Robinson, Connie R.; Pegram, G. Vernon; Hyde, Pam R.; Beaton, John M.; Smythies, John R. Neurosciences Program and Department of Psychiatry, University of Alabama in Birmingham, Birmingham, AL The effects of nicotinamide upon sleep in humans. *Biological Psychiatry* (Amsterdam). 12(1):139-143, 1976.

The effects of nicotinamide upon sleep process in man was studied in six subjects with normal sleep patterns and two subjects with moderate to severe insomnia. For all subjects, there was a significant increase in rapid eye movement (REM) sleep. The changes in all other stages of sleep were not significant. For insomniac subjects, nicotinamide did not improve sleep within 2 weeks but by the third week of drug ingestion sleep was significantly increased. The results obtained may be explained by the buildup of nicotinamide adenine dinucleotide (NAD) upon nicotinamide ingestion, which then could, by feedback inhibition, slow the activity of tryptophan pyrrolase. 4 references.

001989 Rohrberg, Robert G.; Sousa-Poza, Joaquin F. Department of Psychiatry, Université de Sherbrooke, Sherbrooke, Quebec, Canada Alcohol, field dependence, and dyadic self-disclosure. *Psychological Reports*. 39(3, part 2):1151-1161, 1976.

The relationship between alcohol consumption, cognitive style, and dyadic self-disclosure was studied in 16 dyads. Subjects matched for cognitive style (eight field dependent and eight field independent male medical students) discussed five topics -- three on required topics and two which were free choice. Four subjects in each dyad had consumed .80 ml 94% alcohol per kg body weight; the other half received only a mixer with 4 ml alcohol poured on top. Amount of self-disclosure (total time spent in discussion) was not affected by alcohol ingestion; but over all depth of disclosure, as rated by two judges, was significantly greater in the alcohol condition. For all dyads, both amount and depth of disclosure were significantly greater for free choice topics where field dependent pairs showed a significantly higher amount of disclosure as well as greater depth than field independents. 33 references. (Author abstract modified)

001990 Ruther, E.; Davis, L.; Papousek, M.; Reichinger, M.; Reiter, H.; Rudolph, M. Psychiatrische Klinik der Universität München, Nussbaumstrasse 7, D-8000 Munich 2, Germany /Pharmacological influence of central serotonergic mechanisms on humans and effects on sleep./ Pharmakologische Beeinflussung zentraler serotonerger Mechanismen am Menschen und Auswirkungen auf den Schlaf. *Arzneimittel-Forschung* (Aulendorf). 26(6):1071-1073, 1976.

Three experiments were devoted to the effects of serotonergic mechanisms on sleep. In the first experiment, six healthy

male subjects, 23 to 31 years old, were treated with 300mg/day 5-hydroxytryptophan (5-HTP) for 1 week and 600mg/day 5-HTP for the following 3 weeks, along with 375mg/day of the decarboxylase inhibitor Ro 4-4602 for the entire 4 week period. Slow-wave sleep (stages 3 to 4) were reduced by the drug treatment. Three of the patients developed brief paranoid hallucinations. In the second study, six hospitalized patients, one male and five females, 30 to 50 years old, with paranoid hallucinations, anxiety syndrome, or compulsion syndrome, were treated with 200 to 400mg/day clozapine for 14 days. REM sleep increased from 16% of the total sleep time to 24%, and slow-wave sleep decreased from 8% of the total sleep time to 1%. In the third study, six ambulatory patients, five males and one female, 26 to 48 years of age, who had exhibited narcolepsy for several years, were treated with 40mg/day of the serotonin synthesis inhibitor p-chlormethylamphetamine (PCMA) for 1 to 6 months. Under PCMA, narcoleptic attacks decreased from 106/month under placebo to 30/month, and cataleptic attacks decreased 86%. The implications of the findings for serotonergic functioning are discussed. 14 references.

001991 Saletu, B. Abteilung für Pharmakopsychiatrie, Psychiatrische Universitätsklinik, Lazarettgasse 14, A-1090 Wien, Austria **Psychotropic drugs and the quality of sleep: quantitative neurophysiological and subjective parameters.** *Psychopharmaka und die Schlafqualität: Quantitative neurophysiologische und subjektive Parameter.* *Arzneimittel-Forschung (Aulendorf).* 26(6):1042-1047, 1976.

The effect of psychotropic drugs on sleep was studied between 10 p.m. and 6 a.m. in normal subjects ranging in age from 19 to 50 years old. Antianxiety drugs (diazepam, chlorazepate, fluzepam, methaqualone, alprazolam, and triazolam) reduced stages 2 to 4 sleep and prolonged stage 1 sleep, while REM sleep was reduced. Chlorpromazine caused a reduction in stages 1 and 2 sleep, and an increase in stages 3 and 4 sleep, while total REM sleep and number of REM cycles and bursts were increased. In schizophrenic patients, thiothixene, fluphenazine, haloperidol, molindone, and thioridazine increased REM sleep, and decreased deep sleep in low doses and increased deep sleep in higher doses. Tricyclic antidepressants decreased stage 1 sleep and increased stages 2 to 4 sleep; both imipramine and amitriptyline reduced REM sleep. Antianxiety drugs caused a decrease in EEG delta and theta waves, and an increase in beta waves and a decrease in amplitude. Antipsychotic drugs caused a decrease in delta and theta, and an increase in beta waves. Antidepressants caused an increase in delta waves and a decrease in alpha waves. Patients on antianxiety drugs had the best quality of sleep. Subjective ratings of sleep quality after taking antianxiety drugs did not correlate well with objective ratings. Sleep quality seemed worse after taking antidepressants. 15 references.

001992 Salvesen, Christen. Bergen, Norway **Experiences with the use of depot neuroleptics in psychiatric after-care. The organization and results of treatment with pipotiazine palmitate in 3-4 years.** *Acta Psychiatrica Scandinavica (Kobenhavn).* Supplement 265:21-22, 1976.

A summary of a report on the use of depot neuroleptics in long-term psychiatric aftercare, given at a symposium on psychiatric prevention and crisis intervention held in June 1976 at Turku, Finland, is presented. Reporting on the experiences at the aftercare department of the Neevengarden Hospital, Bergen, Norway, continuous medication, combined with psychotherapy and rehabilitation, are considered necessary to prevent relapses in the aftercare of chronic psychotic patients.

Drug deviation is reported to be highest when supervision is lowest, and increases among outpatients and with the time elapsed since hospitalization. Long-acting injectable neuroleptics such as pipotiazine palmitate are characterized as a significant advance in aftercare treatment.

001993 Sato, Taizo; Mori, Yoji; Yamazaki, Tomotake. Department of Neurology, Medical School, Juntendo University, Tokyo, Japan **Effects of L-DOPA on sleep in Parkinsonism.** *Clinical Electroencephalography (Osaka).* 18(6):367-372, 1976.

The effects of L-DOPA on the sleep of five victims of Parkinson's Disease (average age 56) is reported. Dosage began at 1.8gr and was gradually increased to 3.0gr. These results were compared with those of administration to normal persons with the following results: overall sleep time was reduced, with stage 1 increasing, and stages 2, 3, and 4 reduced; more waking periods at night were noted; and REM frequency was increased. Compared with previous sleeping patterns, administration of 1.8gr of the drug decreased overall sleeping time, increased stage 1 sleep, decreased REM frequency, reduced periods of awakening, and had a tendency to regulate sleep periodicity. With 3.0gr administration, the tendencies for regulating periodicity and reducing periods of awakening were further strengthened. 26 references.

001994 Scarone, S.; Spoto, G.; Penati, G.; Canger, R.; Moja, E. A. Istituto di Clinica Psichiatrica, Università di Milano, Via G. Besta 1, I-20161 Milano-Affori, Italy **A study of the EEG sleep patterns and the sleep and dream experience of a group of schizophrenic patients treated with sulpiride.** *Arzneimittel-Forschung (Aulendorf).* 26(8):1626-1628, 1976.

Modifications in EEG sleep patterns following long-term treatment with sulpiride in schizophrenic patients were studied. Subjects were 5 male schizophrenic inpatients between 20 and 35 years of age, who had no primary sleep disorders nor specific medical disturbances. EEG, EMG, and EOG were recorded on the 3rd and 4th nights of sleep, and sulpiride was given on days 5 to 40, with EEG, EMG, and EOG recorded again on the 39th and 40th nights of sleep. Sulpiride did not cause significant change in total sleep time, but light sleep (stages I-II) time was decreased and slow wave sleep (stages III-IV) was increased. Patients reported reduction in difficulty in falling asleep and improvement in dream recall. There was an increase in sleep onset time and a decrease in the number of awakenings during the night. No change in the amount of REM sleep was observed. 21 references.

001995 Seppala, T. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10 A, Helsinki 17, SF-00170, Finland **Effect of chlorpromazine or sulpiride and alcohol on psychomotor skills related to driving.** *Archives internationales de Pharmacodynamie et de Therapie (Ghent).* 223(2):311-323, 1976.

A double-blind cross-over trial was conducted with 20 healthy paid volunteers for the evaluation of the subacute effects of chlorpromazine (CPZ) and sulpiride, in oral doses used for anxious outpatients, alone and in combination with alcohol, on psychomotor skills related to driving. After the neuroleptics alone, reaction and coordination skills, but not attention, were slightly impaired. Both drugs interacted additively with alcohol. The combined administration of CPZ and alcohol led to inaccuracy, a slowing of reactions, and impaired proprioception and coordination. The combination of sulpiride and alcohol increased the error rate in the choice reaction test and impaired coordination in the coordination test. It is concluded that the psychomotor decrement that occurs after 2

weeks of treatment with small doses of CPZ may affect the ability to control a motor vehicle, and that concomitant use of alcohol with CPZ or sulpiride may cause some extra risk. 29 references. (Author abstract modified)

001996 Sheard, Michael H.; Marini, James L.; Bridges, Carolyn I.; Wagner, Ernest. Department of Psychiatry, Yale University School of Medicine, 34 Park Street, New Haven, CT 06508 **The effect of lithium on impulsive aggressive behavior in man.** *American Journal of Psychiatry*. 133(12):1409-1413, 1976.

A double-blind, placebo controlled study of the effect of lithium on aggressive behavior was conducted. The 66 subjects, prisoners in a medium security institution, ranged in age from 16 to 24 years, were physically healthy and nonpsychotic, and had histories of chronic impulsive aggressive behavior. Subjects received lithium or placebo daily for up to three months. There was significant reduction in aggressive behavior in the lithium group as measured by a decrease in infractions involving violence. It is suggested that lithium can have a clinically useful effect upon impulsive aggressive behavior when this behavior is not associated with psychosis. 21 references. (Author abstract)

001997 Smith, J. R.; Karacan, I.; Keane, B. P.; Yang, M. Department of Electrical Engineering, University of Florida, Gainesville, FL 32611 **Automated sleep EEG analysis applied to the evaluation of drugs: illustration by study of clorazepate dipotassium.** *Electroencephalography and Clinical Neurophysiology (Amsterdam)*. 41(6):587-594, 1976.

An automated sleep electroencephalograph (EEG) analysis system was used to evaluate the effects of clorazepate dipotassium in normal, young adult male subjects. The subjects slept in the laboratory for 18 consecutive nights. On days 8 through 15, 7.5mg of clorazepate was administered three times daily; on days 5 through 7 and 16 through 18, placebo was administered. Clorazepate reduced alpha and delta activity, increased beta activity, and increased the number of spindles. The effects generally persisted through the placebo recovery period. It is suggested that sleep EEG waveform descriptors are sensitive indicators of drug activity and that beta activity in particular may be useful in the detailed description of various drug effects. 20 references. (Author abstract modified)

001998 Spring, Carl; Yellin, Absalom M.; Greenberg, Lawrence. Department of Education, University of California, Davis, CA 95616 **Effects of imipramine and methylphenidate on perceptual-motor performance of hyperactive children.** *Perceptual and Motor Skills*. 43(2):459-470, 1976.

Perceptual/motor effects of imipramine and methylphenidate were evaluated in a double-blind study of 47 hyperactive children to determine the efficacy of these drugs in treating hyperactivity. No effects were found for imipramine, although methylphenidate improved performance on several tests. Improvement due to methylphenidate was not related to base-line scores. A discriminant function was computed to compare baseline perceptual motor scores of the hyperactive and 41 normal children. Only half of the hyperactive children were clearly discriminated from normal children by the discriminant function. The digit span test, which was not sensitive to methylphenidate, effectively discriminated hyperactive from normal children. 24 references. (Author abstract modified)

001999 Stokes, Peter E.; Kocsis, James H.; Arcuni, Orestes J. Payne Whitney Clinic, 525 E. 68th Street, New York, NY

10021 Relationship of lithium chloride dose to treatment response in acute mania. *Archives of General Psychiatry*. 33(9):1080-1084, 1976.

The relationship of lithium chloride treatment dose to steady state serum lithium levels and clinical response were examined in 68 manic inpatients. High and medium lithium chloride doses were more efficacious than placebo as determined by decrements in global mania ratings. A low dose was not found to be more efficacious than placebo. The proportion of patients with improved manic ratings increased markedly as a function of increased steady state serum lithium level. 10 references. (Author abstract modified)

002000 Strasser, H.; Muller, K.-W.; Muller-Limmroth, W. Institut für Arbeitsphysiologie der Technischen Universität München, Barbarastr. 16/I, D-8000 München 40, Germany **Effects of two different doses of an antidepressant compared to placebo on tracking behavior in humans./ Experimentelle Untersuchungen des Regelleistungsverhaltens zur Wirkungs-differenzierung eines Antidepressivums in verschiedener Dosierung im Vergleich zu Placebo.** *Arzneimittel Forschung (Aulendorf)*. 26(12):2235-2242, 1976.

The effects of 200mg doses and 400mg doses of mefexamide were compared to those of a placebo on performance of a tracking task by healthy, pretrained subjects. Compared to placebo, the 200mg dose of mefexamide produced slight improvements in tracking while the 400mg dose of the drug deteriorated tracking performance significantly. 19 references. (Journal abstract modified)

002001 Tinklenberg, Jared R.; Roth, Walton T.; Kopell, Bert S. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Marijuana and ethanol: differential effects on time perception, heart rate, and subjective response.** *Psychopharmacology (Berlin)*. 49(3):275-279, 1976.

Performance on a time production task, heart rate, and subjective responses were studied in 12 male subjects given oral doses of marijuana, ethanol and placebo, on 3 testing days which were each separated by 1 week. Orders were balanced across subjects and testing conditions were double-blind. Compared to ethanol and placebo, marijuana induced a significant under production of time intervals, suggesting an acceleration of the internal rate of time perception. The onset of this acceleration of time sense in which geophysical time seemed to pass slowly corresponded with the characteristic increase in heart rate and the onset of the subjective feelings of drug effects. Initial phases of alcohol intoxication were associated with opposite effects on the time production task. These findings replicate previous work and indicate that an easily administered time production task provides a consistent, nonmotor measure of acute marijuana intoxication and also reflects ethanol intoxication. 32 references. (Author abstract)

002002 Warburton, D. M.; Brown, K. Department of Psychology, Reading University, Reading, England **Effects of scopolamine on a double stimulus discrimination.** *Neuropsychopharmacology (Oxford)*. 15(11):659-663, 1976.

Subjects were trained with a light, a temporal cue, and light/temporal cue combination as discriminative stimuli. These groups were tested with doses of scopolamine and it was found that the groups trained with one cue were more sensitive to the drug than the double cue group, although their predrug responding was comparable. A similar pattern was found among individuals in the double stimulus group where

there was a significant correlation between dependency on a single cue, as shown in transfer tests, and drug sensitivity. These results were interpreted in terms of drug induced changes in stimulus sensitivity due to a modification of the neural mechanisms controlling attention. 15 references. (Author abstract)

002003 Wilson, Allan; Davidson, William J.; White, John. Department of Psychiatry, University of Manitoba, 770 Bannatyne Avenue, Winnipeg, Canada R3E 0W3 **Disulfiram implantation: placebo, psychological deterrent, and pharmacological deterrent effects.** *British Journal of Psychiatry* (London). 129(9):277-280, 1976.

Twenty alcoholic patients were given either disulfiram implants or sham operations to examine the placebo, psychological deterrent, and pharmacological deterrent effects associated with implanted disulfiram. Ethanol challenges elicited no disulfiram ethanol reactions (DERs), indicating that at the time of the challenge neither a pharmacological deterrent nor a placebo effect was operating. Of the patients who resumed drinking, only those with disulfiram implants experienced DERs. Sham operation subjects continued to drink after their first postchallenge drink; four of five disulfiram implant recipients remained abstinent following their experience of a DER. It is concluded that the pharmacological deterrent effect of the disulfiram implant may have been underestimated in previous reports. 4 references. (Author abstract modified)

002004 Wilson, G. Terence; Lawson, David M. Alcohol Behavior Research Laboratory, Rutgers, University Building 3530, Busch Campus, New Brunswick, NJ 08903 **Expectancies, alcohol, and sexual arousal in male social drinkers.** *Journal of Abnormal Psychology*. 85(6):587-594, 1976.

The behavioral and pharmacological effects of alcohol on sexual arousal were studied in 40 undergraduate males. Subjects were randomly assigned to one of two expectation conditions in which they were led to believe that they were drinking a beverage containing either vodka and tonic or tonic only. Half of the subjects in each condition drank only vodka, while the other half drank only tonic. Measure of penile tumescence taken after drinks, while subjects were viewing two erotic films, failed to reveal any effect of alcohol per se; but there were significant effects of expectation on penile tumescence during films containing both heterosexual and homosexual interactions. Subjects who believed they had consumed alcohol manifested significantly greater sexual arousal than those who believed they had tonic. Although no consistent effects were observed on additional psychological or physiological measures of sexual arousal, there was a significant positive correlation between self-report measures of sexual arousal and penile tumescence. 20 references. (Author abstract modified)

002005 Wittenborn, J. R.; Flaherty, Charles F., Jr.; McGough, W. Edward; Bossange, Kent A.; Nash, Ralph J. Interdisciplinary Research Center, Rutgers University, New Brunswick, NJ 08903 **A comparison of the effect of imipramine, nomifensine and placebo on the psychomotor performance of normal males.** *Psychopharmacology* (Berlin). 51(1):85-90, 1976.

The effects of imipramine, nomifensine and placebo administered in early morning, late morning and midafternoon on cognitive and psychomotor performance by normal volunteers were assessed. Relative to placebo or nomifensine, imipramine had a clearly detracting effect in most of the tests. Drowsiness was reported more often in the imipramine group than in the two other groups combined. 18 references. (Author abstract modified)

002006 Zimmermann-Tansella, Christa; Tansella, Michele; Lader, Malcolm. Istituto di clinica Psichiatrica di Verona, Università di Padova I-37100 Verona, Italy **The effects of chlordesmethyldiazepam on behavioral performance and subjective judgment in normal subjects.** *Journal of Clinical Pharmacology*. 16(10, part 1):481-488, 1976.

The residual effects of two doses of chlordesmethyldiazepam administered at bedtime on a variety of behavioral tasks and subjective ratings were determined approximately 12 hours after administration to normal subjects and compared with those of amobarbital sodium and a placebo. The 2mg dose of chlordesmethyldiazepam caused more drowsiness on awakening and affected performance on problem-solving tasks, but did not affect motor performance. Self-ratings of alertness were also impaired. Both the 1mg dose of chlordesmethyldiazepam and amobarbital were almost devoid of such effects. Very few drug effects on test anxiety and judgment of performance were discerned. 14 references.

15 TOXICOLOGY AND SIDE EFFECTS

002007 Adriani, John; Naraghi, M. Department of Anesthesiology, Charity Hospital, New Orleans, LA **Clinical use of narcotics.** *Connecticut Medicine*. 40(11):745-750, 1976.

It is contended that Innovar, a fixed ratio combination of fentanyl and droperidol, a butyrophenone, which has been widely promoted for anesthetic procedures, is less than safe. It is asserted that the drug has been responsible for cardiac arrests due to respiratory depression, and that spasticity of the thoracic muscles caused by the fentanyl and hypotension due to overdosage of droperidol when the drug has been used in successive increments throughout a surgical procedure, have occurred. It is advised that other, safer drug combinations are available. 19 references.

002008 Alexander, Carl S. Veterans Administration Hospital, Minneapolis, MN **Epinephrine not contraindicated in cardiac arrest attributed to phenothiazine.** *Journal of the American Medical Association*. 236(4):405-406, 1976.

The notion that epinephrine is contraindicated in cardiac arrest attributed to phenothiazine is argued against. The theory behind the expressed contraindication is based on the mechanism of lowering blood pressure by epinephrine in a system already lowered in pressure by phenothiazine effects. The further drop in blood pressure is said to produce a reflex tachycardia that will disappear with continued use of the drug. In the absence of direct authority on contraindication of epinephrine in cardiac arrest induced by phenothiazine, a treatment is suggested. If a blow to the precordium does not immediately restore heart beat, give epinephrine by intracardiac injection and also begin a levarterenol bitartrate intravenous drip in an attempt to overcome the alpha blockade and to restore blood pressure. Intravenous administration of calcium gluconate is also recommended, as well as cardiorespiratory resuscitative measures. 1 reference.

002009 Alpert, Murray; Diamond, Florence; Laski, Edward M. Department of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Anticholinergic exacerbation of phenothiazine-induced extrapyramidal syndrome.** *American Journal of Psychiatry*. 133(9):1073-1075, 1976.

A tremographic study was performed to record the bilateral digital tremor of a patient (diagnosed as schizoaffective and depressed) showing extrapyramidal motor disturbance after

withdrawal from combined therapy with chlorpromazine, trifluoperazine and trihexyphenidyl. Changes in the amplitude of tremor correlated with clinical ratings of extrapyramidal disturbance. Administration of trihexyphenidyl alone produced a paradoxical increase in tremor. Changes in the amplitude and in the spectrum of tremor were similar to the bipolar paradoxical changes seen during alcohol withdrawal and during intoxication with an anticholinergic psychotogen. It is suggested that a special vulnerability to alterations produced in central neurotransmitter metabolism by psychotropic drugs may explain the idiosyncratic response of this patient. 17 references. (Journal abstract modified)

002010 Ananth, J. Department of Psychiatric Research and Education, St. Mary's Hospital, Montreal, Quebec, Canada **Side effects on fetus and infant of psychotropic drug use during pregnancy.** *International Pharmacopsychiatry* (Basel). 11:4246-260, 1976.

Research studies and reported case studies of the side-effects of the use of psychotropic drugs during pregnancy upon both the fetus and infant were reviewed. Maternal ingestion of some psychotropic drugs for the treatment of emotional as well as other disorders is shown to produce, in the fetus, various side-effects including withdrawal symptoms. Withdrawal signs in the fetus have been reported from the maternal intake of opiates, hypnotics, analgesics, and tricyclic antidepressants. Other side effects including cyanosis, flaccid muscle tone, drowsiness, teratogenesis, edema, goiter, thrombopenia and convulsions can occur from the maternal ingestion of lithium, antidepressants, anxiolytic sedatives, anticonvulsants and bromides. Even though these drugs are generally considered safe when properly used, it is felt that they should be administered to pregnant women only when absolutely needed. 90 references. (Author abstract modified)

002011 Bakker, Jaap B.; Peppinkhuizen, Lolke. Psychiatric Department, Erasmus University, Rotterdam, Netherlands **More about the relationship of lithium to psoriasis.** *Psychosomatics*. 17(3):143-146, 1976.

Side-effects that have been reported with the use of lithium in the treatment of manic-depressive psychoses are discussed; and a review of previously reported dermatological disturbances associated with lithium therapy is presented. The case histories of four manic-depressive patients in whom the appearance or severity of psoriasis was associated with lithium treatment are presented. The effects of lithium on the various organ systems and on the adenylyclase/cyclic AMP system are discussed in relation to the possible role of this system in psoriasis. It is suggested that the inhibitory effects of lithium on the already deficient adenylyclase/cyclic AMP system in the psoriatic derma may lead to the appearance or exacerbation of psoriasis in some patients. 18 references.

002012 Barraclough, B. M. Clinical Psychiatry Unit, Graylingwell Hospital, Chichester, Sussex PO19 4PQ, England **Paraquat poisoning.** *Lancet* (London). No. 7973:1353, 1976.

Mortality statistics for paraquat poisoning in England and Wales are cited to place paraquat fatalities in perspective. For the 5 years 1969 to 1973 only 54 paraquat deaths were reported (0.002% of all deaths and 0.4% of all poisoning deaths). However, in 1973 there were 430 newspaper articles on paraquat poisoning, in 1974 there were 608 newspaper articles, and in 1975 there were 673 newspaper articles. It is suggested that excessive publicity of this numerically unimportant cause of death is undesirable on a number of counts: 1) a useful herbicide may unjustifiably get a bad name resulting in unreasonable

pressure for restriction; 2) it is possible that publicity, by drawing attention to a particular chemical, may cause suicide by imitation - in fact, the number of paraquat suicides show some increase over the 5 years: 30 of the 54 were suicides, and there are open verdicts in 9 deaths.

002013 Bauscher, John; Goldstein, Howard S.; Aronson, Mark D. Department of Medicine, University of Vermont College of Medicine, Burlington, VT 05401 **"Pseudo-giant P-waves" and pericardial friction rub following chlorpromazine therapy.** *American Journal of the Medical Sciences*. 272(3):357-359, 1976.

A patient is presented who manifested two previously undescribed complications of chlorpromazine therapy: a transient pericardial friction rub and pseudo/giant P-waves. After slowing of the heart rate, the giant P-waves proved to be superimposed U and P-waves. The patient's history demonstrates the protean and at times unusual complications of chlorpromazine therapy and illustrates the dramatic therapeutic effects diphenhydramine may have in reversing some of this toxicity. 11 references. (Author abstract)

002014 Belmaker, R. H.; Ebstein, R.; Rimón, R.; Wyatt, R. J.; Murphy, D. L. Jerusalem Mental Health Center - Ezrath Nashim, P.O.B. 140, Jerusalem, Israel **Electrophoresis of platelet monoamine oxidase in schizophrenia and manic-depressive illness.** *Acta Psychiatrica Scandinavica* (Kobenhavn). 54(1):67-72, 1976.

The possibility that qualitative genetic enzyme abnormalities of monoamine oxidase (MAO) could be responsible for the different enzyme activities of platelet MAO in different populations was investigated. Polyacrylamide gel electrophoresis of platelet MAO from 10 manic-depressive, 12 schizophrenic, and 11 normal individuals revealed no genetic mutant forms. 27 references. (Author abstract modified)

002015 Bien, Ralph D. no address **Cogwheel rigidity early in lithium therapy.** *American Journal of Psychiatry*. 133(9):1093-1094, 1976.

In a letter to the editor, the development of cogwheel rigidity during the fourth week of lithium therapy in a patient having no other signs of lithium toxicity is reported. The patient had been diagnosed as bipolar manic-depressive. The rigidity did not respond to benzotropine or diphenhydramine but was relieved after a reduction in lithium dosage. The patient had been taking thiothixene but the drug had been discontinued 1 week prior to the onset of symptoms. It is suggested that cogwheeling should be considered as a possible initial sign of lithium toxicity. This report of cogwheel rigidity developing early in lithium therapy contradicts the statement by B. Shopsin and S. Gershon that this effect occurs during long-term lithium maintenance therapy.

002016 Bolm, W. Hauptstrasse 74, 1000 Berlin 41, West Germany **/Psychiatric pharmacotherapy in renal insufficiency.** *Psychiatrische Pharmakotherapie bei Niereninsuffizienz.* *Medizinische Welt* (Stuttgart). 27(10):478-480, 1976.

The effects of chemotherapy with psychotropic drugs during renal insufficiency are reviewed in 41 cases selected from the literature. Selection criteria included: 1) administration of a neuroleptic or tricyclic drug for more than 20 days or until discontinued because of strong side-effects; 2) pathological isotopic nephrogram; 3) more than 1.5mg% creatinine in the blood serum; 4) principal diagnosis of a psychiatric disorder. Between 1966 and 1975 a group of 22 patients with serum

creatinine level over 1.5mg% and another group of 19 patients with pathological ING but normal serum creatinine were compared. Contrary to expectations there was no significant difference in the reported frequency of side-effects between the two groups. There was greater frequency of urine retention in the group with more serious renal disorders, which could be a side-effect of the chemotherapy, but it also may have been due to the higher dosage and older age of the patients. Another possibility is that renal insufficiency may produce central nervous symptoms that are mistaken for side-effects of the psychotropic drugs. This study has many limitations and further studies with specific drugs in patients with healthy kidneys and patients with renal disorders are desirable. 12 references.

002017 Bonkowsky, Herbert L.; Brisbane, Jane. Veterans Administration Hospital, White River Junction, CT 05001 Colitis and hepatitis caused by methyldopa. *Journal of the American Medical Association*. 236(14):1602-1603, 1976.

It is reported that acute, severe colitis and hepatitis developed in a 55-year-old man on two occasions after administration of methyldopa. The patient also contracted fever, skin rash and eosinophilia, suggesting drug allergy. All symptoms and signs remitted after the drug was withdrawn. It is concluded that methyldopa is capable of producing acute colitis as well as the previously recognized hepatitis. 9 references. (Author abstract modified)

002018 Borg, Stefan; Thunell, Stig; Akerman, Anders. Psykiatriska kliniken, S:t Gorans sjukhus, Box 12500, S-112 81 Stockholm, Sweden /Correlation between injuries due to accident and use of alcohol or drugs./ Forekomst av alkohol och psykofarmaka hos patienter med olycksfallsskador pa en kirurgisk akutmottagning. *Nordisk Psykiatrisk Tidsskrift* (Kungsholmen). 30(2):113-120, 1976.

The correlation between injuries due to accidents and use of drugs is examined. Between 1972 and 1973, 12 representative days were picked out when urine samples and blood samples were taken for toxicological analysis. During that period, the hospital received 224 patients with injuries due to accidents which had happened within 24 hours and 32 patients with accidents which had occurred more than 24 hours before coming to the hospital. The patients were classified according to: age, sex, day of arrival, origin of injury, locale, and type of injury. The tests of the 224 patients showed alcohol in 15% and drugs in 16%. Barbiturates and benzodiazepine derivatives were predominant. Only six persons had used phenothiazine derivatives. Among the 32 patients, only 2 had alcohol in blood while 8 showed drugs in blood or urine. 7 references.

002019 Bourgeois, M.; Graux, C.; Arrethche-Berthelot, N. UER de Psychiatrie, Universite Bordeaux II, Bordeaux, France /Neuroleptic tardive dyskinesias: study of 1660 patients in a psychiatric hospital./ Les dyskinesies tardives des neuroleptiques: enquete sur 1660 malades d'hospital psychiatrique. *Annales Medico-Psychologiques* (Paris). 1(5):737-746, 1976.

A survey of 1660 psychiatric patients in two psychiatric hospitals to study the occurrence of tardive dyskinesia is reported. In the first hospital, tardive dyskinesia was found in 62 of 980 patients. Most of the patients were over 50 years old and had been on major tranquilizers for 1 to 10 years. Half the patients had oral dyskinesia alone and half had oral dyskinesia combined with a diffuse choreiform syndrome. The severity of the dyskinesia was minor in half the patients and moderate or major in the other half. Diagnoses were schizophrenia in 16, chronic delirium in 13, mental retardation in 4, dementia in 14,

depression in 10, neurosis in 4, and epilepsy in 1. Of the 62 patients, 45 had also received antiparkinson drugs and 17 had not. In the second hospital, 58 out of 680 patients had tardive dyskinesia. All but seven patients were over age 40. Duration of major tranquilizer treatment was from less than 10 years to more than 20 years. A total of 22 patients also had a diffuse choreiform syndrome. The dyskinesia was permanent in 38 patients and intermittent in 20. Diagnoses were schizophrenia in 19, delirium in 15, mental retardation in 13, dementia in 7, manic-depressive psychosis in 3, and neurosis in 1. Only 5 patients were not still receiving major tranquilizers, and 57 were still receiving antiparkinsonian drugs.

002020 Bragonier, J. Robert. Outpatient Services and Family Planning, Harbor General Hospital, Torrance, CA Influence of oral contraception on sexual response. *Medical Aspects of Human Sexuality*. 10(10):130, 133-137, 143, 1976.

The influence of oral contraception on sexual response and libido has been examined in a review of available research data presenting critical data assessment. Four studies are reported as demonstrating the spontaneous prevalence of many complaints commonly attributed to oral contraceptives, thus invalidating the exclusive cause and effect relationship proposed. Other studies have reported no libidinal changes and some positive effects. Studies which demonstrate an adverse effect of oral contraceptives on libido and sexual response are shown to be biased toward finding such effects and random effects are also noted. Some tentative conclusions on the influence of oral contraception on sexual responses are offered: the majority of oral contraceptive users have increased frequency of intercourse with significant incidence of depression among those who do not; male partners may be the more crucial determinant in coital frequency whether or not oral contraceptives are used; it is not clear whether libido is increased or decreased in oral contraceptive users; pill use cannot be expected to enhance previously dysfunctioning sexual performance; use of oral contraceptives has not caused an increase in extramarital sexual activity or promiscuity; and it is necessary for physicians to take complaints about oral contraceptive use seriously and attempt to resolve them with the user's involvement. 40 references.

002021 Branchey, Marc H.; Charles, Jess; Simpson, George M. Rockland Research Institute, Orangeburg, NY 10962 Extrapyramidal side effects in lithium maintenance therapy. *American Journal of Psychiatry*. 133(4):444-445, 1976.

Thirty six patients who had been maintained on lithium therapy for periods ranging from 6 months to 7 years were neurologically examined to determine the presence of parkinson like side-effects. Only a few patients demonstrated rigidity, including cog wheel rigidity and this was at a low level of severity. These results do not appear to support the previously reported frequent occurrence of cogwheel rigidity in patients on lithium maintenance. 11 references. (Journal abstract modified)

002022 Brown, Alan; Stickgold, Arthur. Department of Psychiatry, UCLA School of Medicine, 760 Westwood Blvd., Los Angeles, CA 90024 Marijuana flashback phenomena. *Journal of Psychedelic Drugs*. 8(4):275-283, 1976.

Thirteen cases of self-diagnosed marijuana flashbacks, defined as spontaneous recurrences of feelings and perceptions similar to those previously induced in the subjects following the use of the drug, are presented and discussed. The cases are divided into five major categories: prolonged anxiety reaction, precipitation of psychotic reaction, hallucinosis,

enhanced appreciation of environmental stimuli, and questionable cases. The cases that were followed did not seem to represent gross psychiatric impairment and cleared with supportive treatment only. It is suggested that the need for antipsychotic medications and traditional psychotherapy would appear obviated, and that the diversity of etiological considerations would mitigate against accepting the self-diagnosis of the user as accurate or even the best approximation available. 16 references.

002023 Burrows, G. D.; Vohra, J.; Hunt, D.; Sloman, J. G.; Scoggins, B. A.; Davies, Brian. Department of Psychiatry, University of Melbourne, Royal Melbourne Hospital, Melbourne, Victoria 3050, Australia **Cardiac effects of different tricyclic antidepressant drugs.** *British Journal of Psychiatry* (London). 129:335-341, 1976.

Effects of tricyclic antidepressants on the heart were studied. Cardiac function was studied in 32 depressed inpatients before, and 2 weeks after starting treatment with nortriptyline, doxepin, imipramine, and amitriptyline. Heart rate increased an average of 9 beats/min in 26 of the patients. There was an increase in the PR interval in all subjects, while the QT interval did not change. Three patients developed incomplete right bundle branch block in the resting EKG. No arrhythmias or ventricular ectopic beats occurred with exercise. These findings did not correlate with plasma levels of nortriptyline; however, nortriptyline had a significantly greater effect on the PR interval than did doxepin. His bundle EKG was done in 14 patients who had taken an overdose of tricyclic drugs, revealing the AH interval was normal in all patients. The HV interval was abnormal and the QRS complex was wide in seven of the eight patients who had taken overdoses of nortriptyline, amitriptyline, or imipramine, but the bundle EKG was also done in 12 ambulatory depressed patients before, and while on nortriptyline. In five patients nortriptyline caused a prolongation of the HV interval. There was a correlation between prolongation of the HV interval and plasma levels of nortriptyline. In one patient, the HV interval was normal on doxepin, but became abnormal on nortriptyline. 14 references.

002024 Burrows, Graham D. Department of Psychiatry, Royal Melbourne Hospital, Victoria 3050, Australia **Psychotherapeutic drugs: how to minimise complications of therapy.** *Current Therapeutics* (Milford). 17(5):49-50, 53-54, 57-60, 63-64, 1976.

Four general categories of psychotherapeutic drugs are discussed with indications for the use of each category in order to minimize therapeutic complications. Knowledge of their pharmacological characteristics, specific uses, and long-term effects is necessary to prevent complications, and individual responsiveness must be monitored. Drugs analyzed included: antipsychotic, antimanic, anti-anxiety, antiparkinsonian, and antidepressant. It is recommended that patients be instructed in: 1) identification of possible side-effects; 2) anticipation of side-effects; and 3) avoidance of overreacting to side-effects. Special problems of the elderly such as diminished ability to eliminate psychotherapeutic drugs are mentioned. 10 references.

002025 Byrd, Gary J.; Kane, Francis J. Department of Psychiatry, Baylor College of Medicine, Houston, TX 77030 **Persistent psychotic phenomena following one dose of pentazocine.** *Texas Medicine*. 72(6):68-69, 1976.

Acute organic brain syndrome was observed in a 52-year-old male following a single 30mg intramuscular injection of pentazocine. The patient had no previous psychotic episodes. He had been taking diazepam for several months as a muscle

relaxant prior to admission for laminectomy, when he was given 30mg pentazocine and 25mg promethazine i.m. Confusion and auditory hallucinations set in within 6 1/2 hours, and psychotic symptoms persisted for 7 days, cleared spontaneously and have not recurred in a year's time. Two mechanisms of psychic dysfunction are postulated: direct response to pentazocine's toxic effect on the CNS, and lowering of normal psychiatric defenses during a period of high stress, allowing normally repressed material to reach consciousness. 5 references. (Author abstract)

002026 Christiansen, C.; Baastrup, P. C.; Transbol, I. Department of Clinical Chemistry, Psychiatric Department O, Glostrup Hospital, DK-2600 Glostrup, Denmark **Lithium, hypercalcaemia, hypermagnesaemia, and hyperparathyroidism.** *Lancet* (London). No. 7992:969, 1976.

The effect of lithium on electrolyte metabolism is controversial, but hypermagnesaemia has been known for years, while hypercalcaemia was recognized more recently. Long-term lithium therapy patients, such as manic-depressives, exhibit raised serum levels of parathyroid hormone (PTH) and calcium, the pattern being characteristic of primary hyperparathyroidism. 5 references.

002027 Coppen, Alec; Ghose, Karabi. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Do tricyclic antidepressants work?** *Lancet* (London). No. 7969:1128, 1976.

Comment is made to the proposed role of antidepressant drugs in reducing drowsiness in depressed patients. The anxiolytic properties of the drugs have been suggested as responsible for this phenomenon, but reexamination of pretreatment and posttreatment data with patients being administered such compounds indicate that corrected side-effects at 2 weeks, including drowsiness, are significantly and negatively correlated with clinical improvement at 6 weeks. The original conclusion that tricyclic antidepressants do not act as nonspecific sedatives was again supported. Interpretation of the data, and the general relation between depression and its alleviation and side-effects, suggest the complexity of this subject and the need for further study.

002028 Cuzzolaro, Massimo; Zerbetto, Riccardo; Caliri, Benedetto. Università di Roma, Cattedra di Psichiatria, Rome, Italy **Can pentazocine be a drug? Observations on the problem of Talwinism.** *La pentazocina puo' essere una droga? Osservazioni sul problema del Talwinismo.* *Rivista di Psichiatria* (Roma). 11(1):78-95, 1976.

The addictive properties of pentazocine, a benzomorphine derivative, are evaluated. Uses of the compound as a substitute for opiates, heroin, morphine, and other drugs are described. Analysis of clinical studies with different groups of drug addicts indicates that the use of pentazocine can be addictive and that it can have diverse side-effects. 19 references.

002029 Davis, Kenneth L.; Berger, Philip A.; Hollister, Leo E. Department of Psychiatry, Stanford University School of Medicine, Palo Alto, CA 94304 **Tardive dyskinesia and depressive illness.** *Psychopharmacology Communications*. 2(2):125-130, 1976.

The occurrence of tardive dyskinesia, which has been regarded as a long term complication of neuroleptic drug administration to patients with the diagnosis of schizophrenia, is reported in neuroleptic treated patients meeting diagnostic criteria for depression. It is suggested that chronically

decreased neurotransmission in the synapse of a patient with depression may contribute to the development of a supersensitive receptor and could explain the occurrence of tardive dyskinesia in these patients. It is recommended that neuroleptic medications should be administered to depressed patients only after tricyclic antidepressants and anti-anxiety drugs are proven ineffective. It is also recommended that in patients with manic-depressive illness, antipsychotic medications should be discontinued as soon as the patient is stabilized on lithium. 5 references. (Author abstract modified)

002030 Dempsey, G. Michael; Dunner, David L.; Fieve, Ronald R.; Farkas, Tibor; Wong, Julia. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 Treatment of excessive weight gain in patients taking lithium. *American Journal of Psychiatry*. 133(9):1082-1084, 1976.

A portion of the literature dealing with weight gain during chronic lithium therapy, and with possible causes of the weight gain, is reviewed. The effectiveness of a calorie restricted, sodium balanced, potassium balanced, and fluid balanced diet in producing weight loss in lithium treated patients was investigated. Six female primary affective disorder patients lost an average of 2.9kg in 10 days. No evidence of lithium toxicity was observed, probably because fluid and electrolyte balance was controlled. 16 references. (Journal abstract modified)

002031 Dencker, S. J.; Bake, B. Department 2, Lillhagen Hospital, P.O. Box 3005, S-422 03 Hisings Backa 3, Sweden Investigation of the orthostatic reaction after intravenous administration of imipramine, chlorimipramine, and imipramine-N-oxide. *Acta Psychiatrica Scandinavica* (Kobenhavn). 54(1):74-78, 1976.

The age matched and sex matched groups of 10 patients each were treated intravenously with imipramine, chlorimipramine, and imipramine-N-oxide, respectively, in increasing doses from 25mg to 150mg or more per day, given as single daily infusions during 1 hour. No systemic changes of heart frequency or blood pressure were found during the infusions, in spite of the high dosage of tricyclic antidepressants given in such a short period. The patients were examined with respect to orthostatic reactions and ECG changes before, after 4 to 5 infusions, and after 8 to 10 infusions. More orthostatic abnormalities and ECG changes were found in the patients treated with imipramine than in those treated with imipramine-N-oxide; there were practically no changes in the chlorimipramine group. However, no statistically significant orthostatic changes were found. 8 references. (Author abstract modified)

002032 Evans, M. A.; Martz, R.; Rodda, B. E.; Lemberger, L.; Forney, R. B. Department of Pharmacology, University of Illinois-Chicago Medical Center, Chicago, IL Effects of marijuana-dextroamphetamine combination. *Clinical Pharmacology and Therapeutics*. 20(3):350-358, 1976.

Under a double-blind, randomized, complete block design, subjects were given either placebo or 10mg/70kg dextroamphetamine sulfate (A) orally followed 90 min later by a marijuana cigarette (M) prepared to deliver 50 microgram/kg delta9-tetrahydrocannabinol (THC). Statistical analyses suggested that heart rate and blood pressure increased in an additive manner when both drugs were given. Electrocardiogram changes, when present, were nonspecific in character and appeared to be associated with marijuana. In a second study, psychomotor performance was evaluated by a similar design using doses of 10mg/70kg of A and M prepared to deliver 25

microgram/kg THC. Impairment was related to smoking of M, and no difference could be distinguished between M alone and M-A combination. Subjective evaluation, as measured by the modified Cornell Medical Index (CMI) demonstrated only additive effects for the combination. 22 references. (Author abstract)

002033 Fann, William E. Baylor College of Medicine, 1200 Moursund, Houston, TX 77025 Pharmacotherapy in older depressed patients. *Journal of Gerontology*. 31(3):304-310, 1976.

Treatment of depression in elderly patients is not generically different from treatment of depression in younger age cohorts. Because of certain age related physical, physiological, and biochemical factors, tricyclic antidepressants are the principal agents in treatment, but their side-effects tend to be magnified in the elderly. Dosage should initially be lower than with younger patients and increased in gradual increments. Lithium, MAO inhibitors, and neuroleptics are appropriate in some cases, but additional precautions are necessary. Because the elderly are liable to multiple system decompensation, they are likely to be prescribed multiple pharmacological agents. Drug interactions involving antidepressant medication present a variety of therapeutic problems and can threaten life. Depression in late life can be treated pharmacologically, but both the therapeutic and deleterious activities of the drugs can be altered by compromised organ systems. 29 references. (Author abstract modified)

002034 Fedotov, D. D.; Gorbunova, N. A.; Chudin, A. S. Moskovskiy nauchno-issledovatel'skiy institut skoroy pomoshchi im. N. V. Sklifosofskogo, Moscow, USSR /Dynamics of mental disorders due to hypnotic and sedative intoxication./ *Dinamika psikhicheskikh rasstroystv pri otravlenii snotovnymi i sedativnymi preparatami. Zhurnal Nevropatologii i psikiatrii imeni S. S. Korsakova* (Moskva). 76(6):904-908, 1976.

In a study of mental disorders due to hypnotic and sedative intoxication 258 patients, 15 to 60 years old, with marked and borderline psychopathic conditions, most of whom had taken toxic doses of these drugs with suicidal intent, were examined. The mental disorders were less differentiated in the acute period and most diverse in the precoma and postcoma stages. The symptomatology depended on the type of drug, intensity of medical procedures, and the mental disease or borderline state itself, which influences the clinical picture at every stage of intoxication. 7 references. (Author abstract modified)

002035 Fleischhauer, J. Psychiatrische Universitätsklinik Basel, Wilhelm-Klein-Strasse, CH-4025 Basel, Switzerland /Are anticholinergics necessary as a long-term therapy in neuroleptic induced parkinson syndrome? A withdrawal study./ *Sind Anticholinergika als Dauerbehandlung beim neuroleptisch bedingten Parkinsonsyndrom notwendig? Eine Absetzstudie. Arzneimittel-Forschung* (Aulendorf). 26(6):1183-1184, 1976.

The withdrawal of antiparkinson medication in 53 schizophrenics receiving major tranquilizers was studied. The 24 males and 29 females ranged in age from 20 to 79 years and 51 took 2 to 10mg/day biperiden and two received 10mg/day trihexyphenidyl. Ten patients had received antiparkinson medication for 3 to 11 months, and the remaining 43 had received it longer than 12 months. The control group of 38 schizophrenics was continued on antiparkinsonian medication throughout the study. Four female patients showed a deterioration following withdrawal of antiparkinsonian medication, and the medication had to be reinstituted. The dose of major tranquilizer had to

be increased in seven patients, and two of these showed an aggravation in parkinsonian symptoms. 5 references.

002036 Floru, Laurette. Immermannstrasse 10, D-4000 Düsseldorf, Germany /Psychotropic drugs and the eye./ *Psychopharmaka und Auge. Arzneimittel-Forschung* (Aulendorf). 26(6):1190-1191, 1976.

The effects of antidepressants and major and minor tranquilizers on the eye are discussed. Early side-effects of the tricyclic and tetracyclic antidepressants are disturbances in accommodation, mydriasis, and closing of the anterior chamber angle (which can lead to glaucoma); late side-effects affect the retina. Early side-effects of the MAO inhibitors are mydriasis, accommodation disorders, glaucoma, optic nerve neuritis, deterioration of vision, and flattening of the electroretinogram; late side-effects are retinal exudates and bleeding and optic atrophy. Lithium causes disorders of accommodation and nystagmus. Early side effects of phenothiazine, thioxanthene, and butyrophenone derivatives are mydriasis, weakness of accommodation, and closing of the narrow angle of the anterior chamber. A late side effect of the major tranquilizers is the formation of melanin deposits in various parts of the eye. Rauwolfia alkaloids cause miosis, reduced intraocular pressure, and ptosis. Minor tranquilizers cause disorders of accommodation, mydriasis, and drop in intraocular pressure. The ocular effects of psychotropic drugs depend mostly on dosage, length of treatment, and the individual reactions of the patient.

002037 Fookes, B. H. Highcroft Hospital, Birmingham B23 6AX, England *Schizophrenia-like reaction to diethylpropion*. *Lancet* (London). No. 7996:1206, 1976.

In a letter to the editor, a case history of a schizophrenic like reaction to diethylpropion is presented. A housewife and secretary, aged 30, who began a course of diethylpropion as 'Tenuate Dospan' in a dose of 75mg daily in the summer of 1975, stopped the drug suddenly after a month, and a week later began to believe that deep spiritual forces were at work, testing her in various ways. Despite her florid symptoms there was very little disturbance and it was possible to treat her on an outpatient basis with intramuscular fluphenazine. Within a fortnight, much of her conversation was normal, and within two months all features of mental illness had disappeared. At that time the story of the course with diethylpropion was revealed. She now remained well for a year; medication had been discontinued for nine months as of this report.

002038 Gatrad, A. R. Pontefract General Infirmary, Southgate, Pontefract, West Yorkshire WF8 1PL, England *Dystonic reactions to metoclopramide*. *Developmental Medicine and Child Neurology* (London). 18(6):767-769, 1976.

Six cases of dystonic reactions following metoclopramide ingestion are briefly discussed. The pathogenesis of this disorder has not as yet been elucidated, but procyclidine given intravenously promptly relieved the symptoms in three cases. Because the diagnosis is often made retrospectively, physicians should be aware of the diverse symptomatology that can be produced by metoclopramide, which acts on the hypothalamus, and consider this in the differential diagnosis of meningitis, tetany, trismus, chorea, acute torticollis, oculogyric crisis and recurrent dislocation of the jaw. 5 references. (Journal abstract modified)

002039 Gaultier, M. Clinique Toxicologique, Hopital Ferand Widal, F-75475 Paris 10, France *Sodium bicarbonate and tricyclic-antidepressant poisoning*. *Lancet* (London). No. 7997:1258, 1976.

The effects of sodium salts, particularly sodium bicarbonate to combat tricyclic antidepressant poisoning is discussed in a brief letter to the editor. With the introduction of sodium salts for severely disordered myocardial conduction, the mortality rate of massive intoxication fell from 15% to less than 3% by 1968. However, the correction of metabolic acidosis by buffers was not considered an important factor, because alkalization, by trometamol for example, has no effect on cardiac troubles. Other experiments have shown that other sodium salts have the same action on myocardial conduction.

002040 Gelenberg, Alan J. no address *More on neuromuscular side effects of antipsychotics*. *American Journal of Psychiatry*. 133(9):1089, 1976.

In a letter to the editor, criticism is offered on two points of H. R. Barton on the neuromuscular side-effects of antipsychotic drugs. In reply to the suggestion that amantadine reduces the effective level of dopamine in pallidostriatal tissue in animals and should be studied as a possible approach to treatment of tardive dyskinesia, it is stated that amantadine has the opposite effect and is useful in treating Parkinson's syndrome, in which dopamine availability appears to be diminished. In reply to the statement that the presence of tardive dyskinesia suggests cellular damage to the brain, it is stated that this has not been conclusively proven. 6 references.

002041 Gerber, Nicholas; Lynn, Robert K. School of Medicine, University of Oregon Health Sciences Center, 3181 S.W. Sam Jackson Park Road, Portland, OR 97201 *Excretion of methadone in semen from methadone addicts; comparison with blood levels*. *Life Sciences* (Oxford). 19(6):787-792, 1976.

The concentration of methadone was measured in the semen of seven methadone maintenance subjects and compared with the concentration of the drug in blood. The daily dose of methadone in these subjects ranged between 20 and 80mg and was administered by mouth in the local methadone clinic in the usual manner. Samples of blood and semen were obtained from each subject 1 to 4 hours after dosage. The concentration of methadone in the blood ranged between 59 and 126ng/ml in six of the volunteers. The concentration of methadone in semen ranged between 73 and 420ng/ml in the seven subjects. The ratio of the concentration of the drug in semen to the concentration in blood ranged from 0.82 to 4.72. Methadone is excreted in small amounts in human semen and is transmitted from male to female during sexual intercourse. The significance of the repeated transmission of methadone and other drugs in the semen to the female is not known, but the possibility of adverse drug reactions has not been excluded. 16 references. (Author abstract modified)

002042 Glassman, Robert B. Department of Psychology, Lake Forest College, Lake Forest, IL 60045 *A neural systems theory of schizophrenia and tardive dyskinesia*. *Behavioral Science*. 21(4):274-288, 1976.

Some systems ideas applied to individual persons were used to try to explain symptoms of schizophrenia and a syndrome of uncontrolled fragments of movement which sometimes occurs as a side-effect of chronic, antipsychotic drug therapy. It is hypothesized that schizophrenia involves a deficiency of inhibition by the frontal cortex, first echelon, on the corpus striatum, second echelon. This results first in insufficiently integrated fragments of behavior, and second in premature associative linkages among active elements. It is hypothesized that by disrupting certain aspects of activity in the corpus striatum, neuroleptic drugs reduce schizophrenic symptoms but also reduce the capacity of the second echelon to inhibit

and integrate the smaller behavioral fragments wired into lower parts of the brain, third echelon. This results in uncontrolled movements. Emphasis is on conceptual decomposition of the integrated behavior of a whole organism into less complex subsystems. Some experimental predictions and predictions about possible therapies are made. 76 references. (Author abstract)

002043 Good, Michael I. Peter Bent Brigham Hospital, 721 Huntington Avenue, Boston, MA 02115 **Catatonialike symptomatology and withdrawal dyskinesias.** *American Journal of Psychiatry.* 133(12):1454-1456, 1976.

A patient who presented catatonialike symptoms and dyskinesias associated with glutethimide discontinuance and antihistamine use is described. It is hypothesized that altered dopamine metabolism may produce some of the unusual neuropsychiatric characteristics of glutethimide withdrawal. Drug withdrawal catatonia may be an additional entity in the differential diagnosis of catatonialike states of organic etiology. The association of a catatonialike state with the withdrawal of glutethimide and the exacerbation of the reaction by use of antihistamines is compatible with the apparent role of striatal or ascending reticular formation elements in catatonia. 28 references. (Author abstract modified)

002044 Grant, Igor; Judd, Lewis L. Department of Psychiatry, University of California, San Diego, La Jolla, CA 92093 **Neuropsychological and EEG disturbances in polydrug users.** *American Journal of Psychiatry.* 133(9):1039-1042, 1976.

A comprehensive longitudinal study of 120 polydrug users, whose primary drugs of use are central nervous system depressants, was undertaken to assess neuropsychological and electroencephalographic (EEG) data. EEG and neuropsychological evaluation of 66 polydrug users revealed that 43% had EEG abnormalities and 45% had neuropsychological impairment 3 weeks after admission to a polydrug study unit. At 5 month followup, 27% of 30 retested subjects were still impaired neuropsychologically. Impairment may be related to extensive involvement with sedatives, alcohol, or heavy polydrug use. It is suggested that cerebral dysfunction in polydrug users might be the result of organicity of intermediate duration and that deficits may be experienced by some beyond 5 months of reduced use or abstinence. Organicity may dictate structured, reality based intervention techniques, especially early in treatment. 24 references. (Journal abstract modified)

002045 Hattori, Eise; Hotta, Norihiro; Araki, Kuniharu. Department of Neuropsychiatry, Kumamoto University School of Medicine, Japan **Three cases of chronic pentazocine (Sosegon, Pentagin) intoxication.** *Psychiatria et Neurologia Japonica (Tokyo).* 78(3):235-241, 1976.

Three cases of addiction to the nonnarcotic pentazocine (sold under the names Sosegon and Pentagin) are reported. One case of minor cognition impairment, rather than acute addiction was noted. After withdrawal, one case experienced hallucinatory odors. All cases showed a general dulling of the emotions upon withdrawal, with one exhibiting near schizophrenia. Withdrawal symptoms tended to be persistent, and left the victim in a neurotic like state. 19 references.

002046 Hawkins, Doris J. Veterans Administration Hospital, 4801 Linwood Blvd., Kansas City, MO 64128 **Acute organic brain syndrome psychosis with methylodopa therapy.** *Missouri Medicine.* 73(8):476, 481, 1976.

The case history of a 51-year-old male who developed acute organic brain syndrome psychosis after methylodopa therapy is presented. Prior to hospitalization he was taking 500mg of methylodopa four times a day. For the first 3 days of his hospitalization, he took 250mg every 6 hours and his disorientation and hallucinations stopped. The patient's methylodopa therapy was discontinued following psychiatric consultation. His hypertension was managed with other drugs. After 48 hours following discontinuation of methylodopa, the patient's delusions began to lessen. By 72 hours, he was able to sleep well without fear of being harmed. He continued to be free of psychiatric symptoms for the remaining week of his hospital stay. In those rare patients who develop psychotic symptoms while being treated with methylodopa (especially if there is no previous psychiatric history), the physician should be alert to the possibility that a drug related psychosis is occurring. 7 references. (Author abstract modified)

002047 Hill, Reba Michels. St. Luke's Episcopal Hospital, PO Box 29269, Houston, TX 77025 **Fetal malformations and antiepileptic drugs.** *American Journal of Diseases of Children.* 130(9):923-925, 1976.

Recent studies pointing to a correlation between congenital malformation and mothers with a seizure disorder are cited. A direct teratogenic effect of diphenylhydantoin has been proposed although anomalies have been reported in the infants of mothers taking other antiepileptic agents, and the prevalence of anomalies with diphenylhydantoin may only reflect a prevalence in the use of this drug. Genetic predisposition for these anomalies is also a possibility. The duration of treatment with anticonvulsant drugs may also be a factor as multiple deficiency states similar to those found in subjects with long-term alcohol abuse, are known to occur. A table showing the similarities in dysmorphic features of infants fetally exposed to long-term alcohol use and long-term anticonvulsant use is given with relevant research references. Whether these anomalies are a direct result of ingestion of the drug or a result of impaired metabolism caused by the drug is not yet known. 19 references.

002048 Holinger, Paul C.; Klawans, Harold L. Institute for Psychosomatic and Psychiatric Research and Training Michael Reese Medical Center, 2929 S. Ellis Ave., Chicago, IL 60616 **Reversal of tricyclic-overdose-induced central anticholinergic syndrome by physostigmine.** *American Journal of Psychiatry.* 133(9):1018-1023, 1976.

A case study of the reversal of anticholinergic drug induced prolonged coma, myoclonus, and choreoathetosis by physostigmine is presented to give support to the anticholinergic basis of the clinical manifestations of overdoses of tricyclic antidepressants and antiparkinson drugs. The report provides information on the role of acetylcholine and dopamine in psychiatric and movement disorders, and illustrates the need for accurate treatment and diagnosis. 52 references. (Journal abstract modified)

002049 Ito, Itsuro; Kato, Hideaki. Department of Psychiatry, Gifu University, Japan **Concerning aspermia noted in persons taking thioridazine.** *Psychiatria et Neurologia Japonica (Tokyo).* 78(3):246, 1976.

Two cases where aspermia side-effects were noted with the use of thioridazine are reported. Both were single males aged 28 and 38 who had been sexually normal until taking thioridazine. In both cases, erection and orgasm were experienced during sex, but aspermia was complained of. Psychological effects in both cases were considered important

in their aspermia. More research into this phenomenon is proposed to determine whether aspermia is physiogenic or psychogenic.

002050 Jus, A.; Pineau, R.; Hazzi, N. no address **Rauwolfia derivatives and breast cancer.** *American Journal of Psychiatry.* 133(4):451-452, 1976.

In a letter to the editor, the hypothesized link between the use of reserpine and other neuroleptics and the incidence of breast cancer in women is examined. It was found that the percentage of women operated on for breast cancer during a 28 year period before the introduction of rauwolfia derivatives and other neuroleptics (1925 to 1953) was not significantly different from that found after the introduction of these drugs (1954 to 1974). From 1954 to 1974, 53 women (aged 31 to 90) were operated on for breast cancer. For each case of breast cancer, a female patient from the same hospital matched for year of operation and for age was selected as a control. The preoperative exposure of these two groups to reserpine was examined, and it was found that the breast cancer group had not been exposed to reserpine more often than the control group. The incidence of breast cancer was also compared in two groups of 70 women each, one treated with reserpine and other neuroleptics and the other with different neuroleptics excluding reserpine. Four women of each group were operated on for breast cancer, and the incidence of breast cancer in the two samples was the same. 6 references.

002051 Kruger, Gerd; Thomas, D. J.; Weinhardt, F.; Hoyer, S. Universitäts-Nervenklinik, D-87 Würzburg, Germany **Disturbed oxidative metabolism in organic brain syndrome caused by bismuth in skin creams.** *Lancet (London).* No. 7984:485-487, 1976.

Two patients are described with an organic brain syndrome thought to be due to bismuth (Bi) absorbed from a skin cream. Both patients had intellectual impairment and memory loss punctuated by periods of confusion, tremulousness, clumsiness, difficulty in walking, and myoclonic jerks. A similar clinical picture has been reported from Australia and France in patients taking insoluble bismuth salts by mouth. Bi was found in cerebral venous blood in both patients and in the cerebrospinal fluid in one. It is suggested that bismuth can cross the blood/brain barrier and disturb oxidative cerebral metabolism, because increased lactate production was found with decreased consumption of oxygen and glucose and lowered cerebral blood flow. 19 references. (Author abstract)

002052 Kunze, Ulf. Psychiatrisches Landeskrankenhaus, Reichenau, Postfach 3000, D-7750 Konstanz 3, Germany **Chronic bromide intoxication with a severe neurological deficit.** *Journal of Neurology (Berlin).* 213(2):149-152, 1976.

A case demonstrating the typical symptoms and signs of chronic bromide intoxication with mental changes, mild to moderate tremor, and some ataxia of gait is discussed. A delirious state developed when the drug was discontinued. Then some unusual features appeared. Severe neurological deficit developed after the delirium had passed and 8 to 10 days after the drug was stopped. The deterioration consisted in the appearance of a marked resting tremor of the head and upper extremities and of a marked cerebellar dysfunction with severe generalized ataxia but without nystagmus. A considerable CSF level was still present 10 days after discontinuation of the drug. Almost nothing is known about bromide action on the cellular level in the CNS other than the suggestion that it may influence synaptic processes by its action on transport systems. The clinical syndrome in this case suggests a

disturbance within a specific transmitter system. The other unusual aspect was the severe visual dysfunction with a permanent deficit. 12 references.

002053 Lechat, P. no address **/Medication: increased vigilance needed./** *Medicaments: vigilance accrue.* *Revue de Geriatrie (Paris).* 1(1):5, 1976.

Need for circumspection in prescribing drugs that can have undesirable effects in geriatric patients, such as beta-adrenergic blockers, tricyclic antidepressants, thiazide diuretics, L-dopa, antidiabetic sulfamides, and anticoagulants is indicated. The tricyclic antidepressants can cause serious cardiovascular complications, and L-dopa can cause mental problems. 1 reference.

002054 Lipper, Steven. Section on Clinical Neuropharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Psychosis in patient on bromocriptine and levodopa with carbidopa.** *Lancet (London).* 2(7985):571-572, 1976.

A case of persistent paranoid schizophreniform psychosis occurring in temporal association with bromocriptine/sinemet treatment for idiopathic parkinsonism in a 47-year-old woman is reported. The patient has been treated with 4g/day levodopa in conjunction with trihexyphenidyl and amantadine before substitution of 25mg/q.t.d. of bromocriptine. Approximately 6 to 9 weeks into treatment, small amounts of levodopa were added to the drug regime to treat side-effects, and sinemet was subsequently substituted for levodopa. The sinemet was ultimately used alone in large doses, and shortly thereafter the patient began to experience symptoms of paranoid delusions, somatic delusions, auditory and visual hallucinations, and inappropriate affect. Psychotic symptoms continued up to 1 year after onset. It is suggested that bromocriptine may act as a partial dopamine agonist, the discontinuation of which may be followed by dopamine receptor hypersensitivity which is similar to the dopaminergic overactivity implicated in the pathogenesis of schizophrenia. The persistence of the psychosis could not be explained, however. It is suggested that bromocriptine and sinemet be administered simultaneously only with great caution. 5 references.

002055 Loudon, J. B.; Waring, H. University Department of Pharmacology, 1 George Square, Edinburgh EH8 9JZ, Scotland **Toxic reactions to lithium and haloperidol.** *Lancet (London).* No. 7994:1088, 1976.

In a letter to the editor the possibility of a toxic neurological reaction following the combined use of lithium and haloperidol in patients with manic symptoms was investigated. Seven patients are described who experienced unexpected side-effects following exposure to this drug combination. One patient who suffered no side-effects is also described. The patients fall into two groups on the basis of dosage of haloperidol and plasma lithium. These results indicate that great care is needed when administering haloperidol in doses greater than 40mg/day when given with plasma levels of lithium much in excess of 1mmol. 5 references.

002056 Lutz, Elmar G. Department of Neuropsychiatry, St. Mary's Hospital, Passaic, NJ **Neuroleptic-induced akathisia and dystonia triggered by alcohol.** *Journal of the American Medical Association.* 236(21):2422-2423, 1976.

A report of neuroleptic induced akathisia and dystonia triggered by alcohol is presented. Subclinical extrapyramidal symptoms caused by phenothiazine or butyrophenone derivatives (such as chlorpromazine, perphenazine, trifluoperazine

hydrochloride, and fluphenazine decanoate) can become manifest during and shortly after the consumption of alcohol. Alcohol appears to lower the threshold of resistance to neurotoxic side effects of previously established neuroleptic drugs. Abstinence from alcohol should be routine advice during neuroleptic psychopharmacotherapy. 1 reference. (Author abstract modified)

002057 Manaka, Shinya; Izawa, Masahiro; Kawasaki, Mineo; Nawata, Hiroshi. Department of Neurological Surgery, Tokyo University, Medical School, Tokyo, Japan **Exacerbation of epileptic attack and EEG due to intoxication of diphenylhydantoin, a case report.** *Clinical Electroencephalography* (Osaka). 18(5):296-300, 1976.

The case of a 75 kg., 31-year-old man who suffered seizures which were apparently related to antiseizure drug intoxication is reported. The man was suffering from epilepsy caused by external injury and was taking a normal dosage of 300mg Diphenylhydantoin (DPH), 100mg Phenobarbital (PB), and 375mg of Primidon (PM). He would have two or three minor attacks of whole body seizures yearly and complained of sleepiness, fatigue, and numbness in the limbs. Abnormal slow brainwaves were also noted. Levels of PB and PM in the blood were not abnormal, but that of DPH was surprisingly 40.9mg/ml. Upon reduction of his dosage of DPH to 200mg and PB to 100mg, his seizures and other side-effects disappeared. This paradoxical seizure activity caused by high levels of DPH in the blood is called the DPH encephalopathy syndrome (cf. Glaser 1972). 18 references.

002058 Margolin, David I. Chicago, IL **Methylphenidate-induced tics.** *Journal of the American Medical Association*. 236(8):917-918, 1976.

Two comments on a published article regarding methylphenidate hydrochloride induced oral/facial tics as well as other induced dyskinesias are made. One, subtle dyskinetic movements in the hyperkinetic child and in this population may easily be obscured and underreported associated with amphetamine or methylphenidate therapies. Two, direct evidence that some hyperkinetic children display decreased and measurable central dopamine activity is available which may reflect denervation hypersensitivity of central dopamine pathways. 6 references.

002059 Marks, P.; Sloggem, J. Cardiac Laboratory, Rm. 319, Page Street Wing, Westminster Hospital, London SW1P 2AP, England **Peripheral neuropathy caused by methaqualone.** *American Journal of the Medical Sciences*. 272(3):323-326, 1976.

Three patients are described who received methaqualone and developed signs and symptoms of peripheral neuropathy. The subsequent improvement after cessation of methaqualone was highly suggestive of a direct toxic action of the drug or one of its metabolites. In one patient methaqualone was recommended with reappearance of signs and symptoms of peripheral neuropathy. Again cessation of the drug caused disappearance of these signs. There was no evidence whatsoever of any electrolyte or metabolic disturbance or any other pathology which might have given rise to this symptom complex. In addition, no other drugs were prescribed besides methaqualone. 5 references. (Author abstract)

002060 Marsden, C. D. University Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, London SE5 8AF, England **Cerebral atrophy and cognitive impairment in chronic schizophrenia.** *Lancet* (London). No. 7994:1079, 1976.

In a letter to the editor the hypothesis is advanced that the cerebral atrophy and cognitive impairment seen among chronic schizophrenics is due to neuroleptic drug therapy rather than to incidental or causal pathology. Chronic tardive dyskinesias, occurring in up to 40% of the patients treated with neuroleptic drugs for long periods of time, is thought to be due to altered sensitivity of the cerebral dopamine receptors on which all neuroleptic drugs act as antagonists. When the neuroleptic drug was stopped chronic tardive dyskinesias often gradually disappeared. But in 50% of the patients, the symptoms remained. It is concluded that if long-term neuroleptic therapy can cause an apparently permanent change in striatal dopamine receptor action, it can be assumed that the same can occur in the mesolimbic cortical dopamine receptors accounting for some of the cerebral atrophy and related cognitive impairment in schizophrenics. 5 references.

002061 Martini, M.; Passero, S.; Martini, A. Ospedale Psichiatrico S. Niccolo, Siena, Italy **Use of dextimide (R 16 470) with extrapyramidal syndromes caused by neuroleptics./ Azione della dextimide (R 16 470) nelle sindromi extrapiramidali da neurolettici.** *Rassegna di Studi Psichiatrici* (Siena). 65(5):997-1031, 1976.

A double-blind study of dextimide was carried out with 40 psychotic patients who were suffering from extrapyramidal side-effects of neuroleptic medication. Subjects were between 31 and 86 years of age and had been hospitalized for a long period of time in the Psychiatric Hospital of S. Niccolo in Siena, Italy. Results showed that dextimide is effective in treating Parkinsonism caused by neuroleptic medication. It is especially significant that dextimide had a particular effect on tremor, muscular rigidity, and dyskinesia and that it had no pejorative collateral effects of its own. 6 references.

002062 Mohamedi, S.; Bathai, H. Pasteurstreet 58, Teheran, Iran **Cardiovascular effects of neuroleptic and antidepressant drugs. Preliminary report./ Kardiovaskulare Wirkungen neuroleptischer und antidepressiver Medikamente: Vorlaufige Mitteilung.** *Medizinische Welt* (Stuttgart). 27(4):168-171, 1976.

Cardiovascular side-effects of the neuroleptics chlorpromazine, perphenazine, and thioridazine and the tricyclics imipramine and amitriptyline were studied in 71 long-term patients at the Roozbek Hospital in Teheran. In general, the side-effects included tachycardia, reduction in both diastolic and systolic blood pressure, lengthening of the QT, ST and T in the EKG and an expansion of the QRS, with symptoms of sympathetic nervous disorder. These side-effects did not necessitate interruption of chemotherapy for any patient, but a controlled study of these medications for their cardiovascular side-effects is in order. Charts showing quantitative data about cardiovascular side-effects in the 71 patients, whose age ranged from under 15 to over 60, are included. 3 references.

002063 Muniz, Carlos; Forman, Arthur J.; Wilder, B. J.; Ramsay, R. Eugene. Department of Psychiatry, University of Florida College of Medicine, Gainesville, FL 32610 **Lithium toxicity with low serum levels: report of a case.** *Clinical Electroencephalography*. 7(1):31-34, 1976.

A case report is presented of a 56-year-old man who developed a clinical picture suggestive of severe lithium toxicity after being administered that drug for depression, even though his serum level was well within the therapeutic range (1.2mEq. per liter). Serial electroencephalographic tracings showed alterations that correlate with the clinical findings. When lithium carbonate was discontinued, signs and symptoms and electroencephalographic abnormalities returned to

normal. It is suggested that in some patients there may be a decrease in the concentration of certain cations in the CNS and lithium is sequestered as a substitute. 7 references.

002064 Munoz, Rodrigo A. Medical Arts Building, 1226 North 8th Street, Sheboygan, WI 53081 **Treatment of tricyclic intoxication.** *American Journal of Psychiatry.* 133(9):1085-1087, 1976.

Eleven supportive and symptom specific measures for the emergency treatment of intoxication with tricyclic antidepressants are outlined. It is reported that physostigmine has been used successfully to treat tricyclic antidepressant poisoning in 15 patients. 15 references. (Journal abstract modified)

002065 Neale, Richard. St Thomas's Hospital, London SE1, England **Attempted suicide in labour.** *British Medical Journal (London).* No. 6005:321-322, 1976.

A case study is presented of an attempted suicide in labor. The 20-year-old unmarried girl had a past history of petit mal epilepsy, intermittent depression, and premenstrual tension. She attempted suicide because a neighbor had told her that a yellow vaccination, taken before she knew she was pregnant, would cause a malformed baby. At the onset of labor, 7 to 8 hrs before delivery, she took a supply of diazepam and amylorbarbitone, which she had hoarded during an 8 day hospital stay prior to onset of labor. The prolonged neonatal depression observed in the baby was presumably due to the diazepam. Since diazepam is commonly given in current obstetric practice, the nursing staff should ensure that the drugs issued are actually taken by any patient who might possibly take an overdose. 5 references.

002066 Neil, John F.; Himmelhoch, Jonathan M.; Licata, Sandra M. University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15261 **Emergence of myasthenia gravis during treatment with lithium carbonate.** *Archives of General Psychiatry.* 33(9):1090-1092, 1976.

A case of a patient with recurrent episodes of severe mania, in which classical manifestations of myasthenia gravis developed for the first time during treatment with lithium carbonate is described. Neurologic symptoms were ameliorated or disappeared shortly after the drug was discontinued or its dosage was reduced. There was no evidence of lithium carbonate toxicity or electrolyte disturbances at any time during treatment. Based on a literature review of animal studies and related clinical reports, a mechanism of peripherally mediated neuromuscular cholinergic insufficiency is proposed. The differential diagnosis of muscle weakness during lithium carbonate administration is discussed. 20 references. (Author abstract modified)

002067 no author. no address **The use of anesthesia in children.** *Medical procedures in children.* *Lancet (London).* No. 7973:1335-1336, 1976.

The use of anesthesia in the treatment of children is discussed, and it is noted that small children are not diminutive adults in their reaction to anesthetic drugs. Syrup of chloral used to be given in large quantities to children about to undergo an unpleasant procedure. Profound sedation, with lytic cocktails (usually a mixture of promethazine, chlorpromazine, and pethidine) or with neuroleptanalgesia, has also been tried, but the prolonged action of these drugs, and occasional hypotension, make them unsuitable. Ketamine has found application in anaesthesia for short procedures, particularly in children for the changing of burn dressings and for

cardiac catheterization. Unfortunately, the administration of this drug is not always trouble free. Patients occasionally become apneic for short periods immediately after injection of the drug. Laryngospasm has been reported, and the drug raises intracranial pressure. The problem of dreams or hallucinations in the postoperative period following ketamine anesthesia is discussed. 10 references.

002068 no author. no address **Sodium bicarbonate and tricyclic-antidepressant poisoning.** *Lancet (London).* No. 7990:838, 1976.

The treatment of tricyclic drug overdose is discussed. Of 12 children with arrhythmias caused by tricyclic antidepressants, 9 responded rapidly to sodium bicarbonate and 2 responded to bicarbonate plus other drugs. Pupils were found to respond to bicarbonate when overdosed with tricyclic drugs. The beneficial effects of bicarbonate are probably due to correction of the acidosis, but they may also be due to an increase in plasma protein binding of the drug. Sodium bicarbonate is thus recommended for treatment of tricyclic drug overdose when metabolic acidosis exists. Poisoning by these drugs now accounts for 9% of all deaths from poisonous solids and liquids. 7 references.

002069 Parker, Elizabeth S.; Birnbaum, Isabel M.; Noble, Ernest P. School of Social Sciences, University of California, Irvine, CA 92717 **Alcohol and memory: storage and state dependency.** *Journal of Verbal Learning and Verbal Behavior.* 15(6):691-702, 1976.

The effects of acute alcohol intoxication on the storage phase of memory were evaluated with two tasks that minimized response retrieval: unpaced paired-associate learning with highly available responses and forced choice picture recognition. Paired-associate learning was impaired by the high dose of alcohol (1.0ml/kg), while the placebo and medium dose (0.5ml/kg) were equivalent. Picture recognition showed a dose dependent decrement. It was concluded that storage processes are sensitive to disruption by alcohol. Alcohol did not produce decrements in memory for the original material when retention was tested 2 weeks later, and there was no evidence for state dependency. 32 references. (Author abstract)

002070 Phillips, P. J.; Bastian, P. D.; Burrow, D. D.; Henschke, P. H.; Waltham, R. D. Royal Adelaide Hospital, Adelaide 5000, South Australia, Australia **Drug-withdrawal syndromes.** *Lancet (London).* No. 7969:1131, 1976.

A classification outline of drugs reported to be associated with withdrawal symptoms is presented. The two part outline includes drugs affecting the central nervous system (narcotics, depressants, sympathomimetics, drugs of pleasure, psychotropic compounds, and antiparkinsonian drugs), as well as other formulations, including analgesics, cathartics, and antihypertensives. Although the list is not considered complete, it draws attention to little known therapeutic problems and reinforces the need for a drug history for each patient and for wide use of devices which give a patient's current drug regimen (e.g. bracelets). Such procedures will help avoid potentially lethal withdrawal syndromes.

002071 Radmayr, E. Bahnhofplatz, A-6850 Dornbirn/Vlb., Austria **Long-term therapy with Sinquan: investigation of tolerance with systematic laboratory control./ Langzeittherapie mit Sinquan: untersuchungen zur Vertraglichkeit unter systematischer Kontrolle der Laborwerte.** *Medizinische Welt (Suttgart).* 27(9):446-447, 1976.

Twenty patients who had received 100mg doxepin (Sinquan) daily from 1968 to the end of 1974 were studied for side-effects with laboratory control of blood and urine parameters. The patients, who were between the ages of 41 and 69 years old, included 19 women and 1 man, were selected on the basis of having a chronically recurring affective psychosis for at least 10 years that was not typical of a manic-depressive psychosis suitable for lithium therapy. Blood pressure, erythrocyte, hemoglobin, and leucocyte count, LDH, urine nitrogen, alkaline phosphatase, SGOT, SGPT, and urine protein, sugar, and bile content were controlled monthly during the 1st year, and four times per year afterward. Statistical analysis of these values showed there was no pathological change in blood chemistry or urine composition after long-term doxepin therapy.

002072 Riley, Terrence; Brannon, William L., Jr.; Davis, William. Dept. of Neurology, National Naval Medical Center, Box 360, Bethesda, MD 20014 **Phenothiazine reaction simulating acute catatonia**. *Postgraduate Medicine*. 60(2):171, 173, 1976.

A case study is reported of a phenothiazine reaction simulating acute catatonia. Following administration of three 10mg doses of prochlorperazine (phenothiazine) over a 6 day period, a 34-year-old woman undergoing treatment for acute myelogenous leukemia suddenly showed signs of motor disturbance and within several hours lapsed into a catatonic like stupor. The patient had received the following medications: 1) methotrexate (enzyme folic acid reductase inhibitor); 2) cytarabine (cytosine arabinoside); and 3) cyclophosphamide and vinblastine sulphate. She had also received whole body irradiation in preparation for a bone marrow transplant. Psychiatric evaluation showed no evidence of psychiatric disorder, and neurological findings had been within normal limits. In spite of two weeks confinement in an isolation tent and a poor prognosis, the patient had remained alert and reasonably cheerful. Twenty four hours after the last of the three doses of prochlorperazine, the patient became listless and finally ceased response to pain in what appeared to be an acute psychotic reaction. The condition was alleviated with the injection of 50mg of diphenhydramine hydrochloride which was also administered for recurrences over the next 36 hours. Permanent relief was obtained with 2mg of benzotropine mesylate twice daily for several days. The patient could recall in detail all occurrences during these episodes and expressed having been greatly distressed by her immobility. Following the patient's death 2 weeks later, a necropsy revealed no gross or microscopic brain lesions. A discussion provides evidence that the catatonia was prochlorperazine induced and speculates as to possible potentiating effect from some of the immunosuppressive medications being administered. 3 references.

002073 Robinson, Donald S.; Barker, Eileen. Clinical Pharmacology Unit, University of Vermont College of Medicine, Burlington, VT 05401 **Tricyclic antidepressant cardiotoxicity**. *Journal of the American Medical Association*. 236(18):2089-2090, 1976.

Effects of tricyclic antidepressants on the heart are reviewed. Dose related EKG changes include prolongation of the PR interval, widening of the QRS complex, and non-specific T-wave changes. Studies of imipramine and its metabolites desipramine, 2-hydroxyimipramine, and 2-hydroxydesipramine, showed substantial cardiotoxicity in dogs at imipramine dosages considered therapeutic in humans. All these substances substantially decreased cardiac output, left ventricular work, and cardiac contractility, and increased peripheral vascular resistance. Children may be more suscepti-

ble to toxic effects because of decreased drug binding to plasma albumen and because of a smaller lipid storage compartment. The rate of drug biotransformation by the liver is enhanced in children, and this could result in increased production of tricyclic metabolites. Therefore, the Food and Drug Administration recommends the pediatric dosage of imipramine not exceed 2.5mg/kg/day in the treatment of enuresis, the only approved pediatric use of tricyclic drugs. When dosages of 200mg/day are exceeded in adults, EKG monitoring should be done during initial tricyclic therapy. EKG monitoring should also be done in patients with preexisting conduction disturbances, arrhythmias, or other symptomatic cardiac disease. 20 references.

002074 Rosser, Rachel. Maudsley Hospital, London SE5, England **Thyrotoxicosis and lithium**. *British Journal of Psychiatry* (London). 128:61-66, 1976.

Two cases of depression in which treatment with lithium was complicated by thyrotoxicosis are presented and the underlying physiological mechanisms discussed. Lithium suppresses thyroid function, so the early stages of thyrotoxicosis may be undetected, and the symptoms and signs of thyrotoxicosis may be confused with the side-effects of lithium. If lithium is withdrawn, severe rebound thyrotoxicosis may occur. Furthermore, some of the side-effects of lithium may be aggravated by thyrotoxicity. Recommendations for routine screening of thyroid function before starting lithium treatment are discussed. 20 references. (Author abstract modified)

002075 Ruger, U. Psychiatrische Klinik der FU, Nussbaumallee 36, 1000 Berlin 19, Germany **Psychological aspects of phasic depression during lithium prophylaxis./Tiefenpsychologische Aspekte des verlaufs phasischer Depressionen unter Lithium-Prophylaxe**. *Nervenarzt* (Berlin). 47(9):538-543, 1976.

A followup study is presented of 20 patients on long-term lithium therapy for phasic depression. A case study of one of the patients is included. Two aspects are investigated: whether there has been a renewed manifestation of endogenous depression, and the nature of the "inner psychological balance," i.e. whether other mental disturbances may occur while on lithium therapy. Results of the Freiburg Personality Inventory (FPI) showed normal values on the depression scale for most of the patients; those not showing normal ranges could be otherwise explained (e.g. a patient with cancer). Eleven of the patients showed extreme FPI values in conflict producing areas which had little correlation with the depression factor. The case study presents one of these: a female patient showing extreme values for the dominance factor while maintaining normal depression values. Although the study reaffirms the fact that lithium affords protection from psychotic decompensation, it seems to lead some to new internal conflicts. These conflicts however can be seen perhaps as stabilizing, and merely neurotic or psychosomatic, rather than psychotic. 10 references.

002076 Shopsin, Baron; Gershon, Samuel. no address **Reply to a letter contradicting the statement that cogwheel rigidity is related to long-term lithium maintenance therapy./Drs. Shopsin and Gershon reply**. *American Journal of Psychiatry*. 133(9):1094, 1976.

In reply to a letter describing a manic-depressive patient who developed cogwheel rigidity during the fourth week of lithium therapy, thus contradicting the statement that this effect is associated with long-term lithium maintenance therapy, it is stated that the thiothixene that the patient had been taking, although discontinued 1 week prior to the onset of symp-

toms, cannot be ruled out as a cause of the rigidity. Because neuroleptics and their metabolites may persist in the body for up to 6 months after discontinuation, extrapyramidal symptoms may occur rapidly after initiation of lithium treatment in patients who had recently received neuroleptics. It is also pointed out that signs of extrapyramidal involvement have previously been reported as symptoms of CNS involvement with acute lithium toxicity and poisoning. 3 references.

002077 Suzuki, Yasuyuki; Morita, Shigeji. Minami Chita Hospital, Japan *On the swelling of the diaphragm among patients taking psychotropic drugs (second report).* *Psychiatria et Neurologia Japonica* (Tokyo). 78(3):246, 1976.

Diaphragm swelling was investigated in 13 patients who were taking psychotropic drugs. A previous report found that this largely occurred in obese patients as well as those with respiration abnormalities. This connection was explored further. More than half of the patients investigated had functional liver abnormalities, and many had high blood sugar levels. Other abnormalities were also discussed. It was concluded that the relationship between these and psychotropic drugs was difficult to establish.

002078 Tobis, Jonathan.; Das, Bodh N. University of California at Irvine, Irvine, CA 92664 *Cardiac complications in amitriptyline poisoning: successful treatment with physostigmine.* *Journal of the American Medical Association.* 235(14):1474-1476, 1976.

Cardiac complications in a 22-year-old woman following a suicide attempt by ingestion of amitriptyline were successfully treated with physostigmine. This is felt to be the first reported case of amitriptyline poisoning in which malignant arrhythmias and conduction effects were successfully relieved in this manner. It is believed that the cardiac disturbances of amitriptyline poisoning occur through competitive blockade of acetylcholine receptors.

002079 Torry, J. M. Department of Forensic Medicine, London Hospital Medical College, London, England *A case of suicide with nitrazepam and alcohol.* *Practitioner* (London). 217(1300):648-649, 1976.

A case is described in which a 55-year-old man committed suicide by taking nitrazepam (Mogadon) and alcohol. Chronic bronchitis was considered to be a major contributory factor. The importance of this case is that it confirms the danger that even safe hypnotics such as nitrazepam can lead to fatalities when taken in certain circumstances. 6 references. (Author abstract modified)

002080 Valdes, Michael E. Albany Medical Center of Union University, Albany, NY 12208 *Post-dopamine ischemia treated with chlorpromazine.* *New England Journal of Medicine.* 295(19):1081-1082, 1976.

In a letter to the editor a case history of a 72-year-old man is presented in order to demonstrate the potential use of chlorpromazine in the treatment of ischemia as a side effect of dopamine. Chlorpromazine drip was instituted for 5.5 hours and, although the patient required high doses of dopamine for 25 additional hours, the digital ischemia did not recur. It is concluded that intermittent bolus administration of chlorpromazine might also be effective. 2 references.

002081 Vivien, P.; Leverger, J.-C.; Allanic, H.; Lorcy, Y. no address *Thyroid insufficiency in the course of lithium therapy./ Insuffisance thyroïdienne en cours de thérapeutique par le lithium.* *Nouvelle Presse Medicale* (Paris). 5(3):147, 1976.

A case report is given of a patient who developed a goiter and a decrease of serum thyroxine levels, but not myxedema, during treatment with lithium. Hypothyroidism due to lithium affects women especially, perhaps affecting women with a latent thyroiditis. Neither age nor duration of treatment has any effect. Cure occurs after stopping lithium treatment or adding thyroid extract. Thyroid function should be studied before and during lithium treatment. A small dose of thyroid extract has been recommended in the course of lithium treatment.

002082 Volk, Walter; Stoll, K.-D. Psychiatrische Klinik, Bürgerhospital, Tunzhofer Strasse 14-16, D-7000 Stuttgart 1, Germany *Double-blind trial of therapy of orthostatic hypotension in psychotics under psychotropic medication./ Doppelblindversuch zur Therapie orthostatischer Dysregulationserscheinungen bei Psychotikern unter psychotroper Medikation.* *Arzneimittel-Forschung* (Aulendorf). 26(6):1188-1189, 1976.

The use of mineralocorticoids and sympathomimetic amines to treat postural hypotension was studied in 13 hospitalized patients who were receiving major tranquilizers in moderate or large doses. The six males and seven females ranged in age from 21 to 62 years, with mean age 33.6 years. One patient had endogenous depression; and the other 12 were schizophrenic. Circulation was measured by the Schellong Test. Patients were treated in double-blind fashion with 9, alpha-fluorohydrocortisone (0.15mg b.i.d. the first week, followed by 0.1mg b.i.d. thereafter), norphenylephrine (15mg b.i.d.), or placebo (1 tablet b.i.d.). After 2 weeks, 9, alpha-fluorohydrocortisone was significantly better than either norphenylephrine or placebo, as measured by the Schellong test. Norphenylephrine was better than placebo, but the difference was not significant. No treatment group experienced side-effects. 15 references.

002083 Wenk, Robert E.; Samano, A. Francisco; Lustgarten, Jack A.; Pappas, N. John. Division of Clinical Pathology, Sinai Hospital, Baltimore, MD 21215 *The contemporary diagnosis of bromism.* *Maryland State Medical Journal.* 25(12):49-50, 1976.

Indications for a diagnosis of bromism are reported and discussed. Spuriously elevated serum chloride values may be the first or only diagnostic sign of bromide toxicity. Newer methods of chloride analysis vary in their response to bromide interference, but the occurrence of bromide in the sera of inpatients is 0.75% in a general hospital and 13.0% in a psychiatric hospital. Because bromism is not obsolete, and because it may mimic other medically or surgically treatable diseases, both the laboratory staff and physician must be alert to suspect it. 6 references.

002084 Wilkinson, I. M. S. Aldenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, England *The influence of drugs and alcohol upon human eye movements.* *Proceedings of the Royal Society of Medicine* (London). 69(7):479-480, 1976.

The effects of alcohol and various drugs on human eye movement is discussed in the light of various research findings. Studies indicate that both saccadic and smooth pursuit eye movements are slowed by the consumption of drugs or alcohol. Oculocephalic eye movement, however, is not seriously impaired by moderate drug or alcohol doses. It is posited that the impairment of saccadic and smooth pursuit eye movements is probably due to the effect of the drugs upon the cerebral cortex since oculocephalic movements remain unimpaired under the same conditions of consumption. 6 references.

16 METHODS DEVELOPMENT

002086 Alfredsson, Gunnell; Wode-Helgödt, Birgitta; Sedvall, Goran. Department of Pharmacology, Karolinska Institutet, S-10401 Stockholm, Sweden *A mass fragmentographic method for the determination of chlorpromazine and two of its active metabolites in human plasma and CSF.* Psychopharmacology (Berlin). 48(2):123-131, 1976.

A mass fragmentographic method for the quantitation of chlorpromazine (CPZ), mono-demethyl-chlorpromazine, and 7-hydroxychlorpromazine in plasma, cerebrospinal fluid, and tissues has been developed. The deuterated analogues of the compounds are used as internal standards. The high specificity was ascertained by multiple ion determination. The method has been applied to the analysis of drug concentrations in plasma and cerebrospinal fluid (CSF) of chlorpromazine treated patients. The amount of CPZ in CSF was about 3% of the plasma level. The CPZ levels in plasma and CSF were significantly correlated. 19 references. (Author abstract)

002087 Bond, Michal R.; Glynn, J. P.; Thomas, D. G. University of Glasgow, Southern General Hospital, Glasgow, G51 4TF, Scotland *The relation between pain and personality in patients receiving pentazocine (Fortral) after surgery.* Journal of Psychosomatic Research (Oxford). 20(4):369-381, 1976.

An investigation was carried out in which a series of patients who had surgery for a prolapsed intravertebral lumbar disc were examined for the effectiveness of a postoperative analgesic drug, pentazocine, prescribed regularly for pain. The patterns of relief gained were related to blood levels of the drug and to personality structure measured by the Eysenck Personality Inventory. The latter comparison was carried out in order to determine whether or not previously detected differences in pain experience and complaint behavior were present and, if so, to what extent. It is concluded that careful attention to the selection of an analgesic and its method of administration reduces the discrepancies in pain levels reported previously in individuals with different personality structures. 10 references.

002088 Cromie, B. W. Hoechst UK Ltd., Hounslow, Middlesex, England *Methodology in double-blind drug trials./ Not so double-blind? British Medical Journal (London).* No. 6011:710, 1976.

The belief that drug trials are double-blind only if all medications under test appear to be identical is disputed. Any method that prevents recognition of a preparation under test by patient or doctor permits a valid double-blind trial. It is not essential for active treatment and placebo to appear to be identical.

002089 Dubenko, E. G.; Nebotov, V. A. Kafedra nervnykh bolezney Khar'kovskogo meditsinskogo instituta. Kharkov, USSR *Periodic structure of physiological and pathological tremor./ O periodicheskoy strukture fiziologicheskogo i patologicheskogo tremora.* Zhurnal Nevropatologii i Psikiatrii imeni S. S. Korsakova (Moskva). 76(7):966-972, 1976.

The theory is proposed that the most informative criterion of the state of the nervous system is frequency characteristics of its processes. Using spectral analysis and intervalography, changes of finger tremor were studied in intellectual and nitroglycerine tests in 45 normals and 15 patients with functional CNS disorders. Results showed spectrum analysis of tremor combined with EMG may be used to analyze the functional status of mechanisms regulating tremor in patients with

nervous system injury and also to evaluate pharmacological reactions during treatment. 31 references. (Author abstract modified)

002090 Hill, Lisa E.; Nunn, A. J.; Fox, Wallace. Medical Research Council, Tuberculosis and Chest Diseases Unit, Brompton Hospital, London SW3, England *Matching properties in double-blind trials./ Not so double-blind? British Medical Journal (London).* No. 6011:710, 1976.

A panel of four observers compared the matching qualities of 22 pairs of medications employed in double-blind investigations. Five pairs of substances were virtually indistinguishable, but in seven, there were differences obvious to all the panel members. Matching properties should not be evaluated casually, but should be investigated in a formal way; however, a small panel of assessors is adequate. 2 references.

002091 Israel, Liliane; Ohlman, T.; Hugonot, R. Service de Geriatrie, CHU de Grenoble, Grenoble, France *Study of the activity of cerebral medications. A new methodology: level of comparative trials./ Etude de l'activite de medications a visee cerebrale. Une nouvelle methodologie: le banc d'essais comparatifs.* Revue de Geriatrie (Paris). 1(1):46-51, 1976.

A new methodology is given for the study of drugs having an effect on the cerebrum. Of seven patient groups, three received cerebral vasodilators, and others received an anti-thrombotic drug, a metabolic activator or placebo, and one group served as control. Patients were evaluated by a sign barrier test, number repetition, object and picture arrangement, Poppelreuter semantic test, coding, word repetition, psychomotor aiming, visual/verbal memory, verbal fluidity, picture arrangement, graphomotor praxia, and ability to recall the tests taken. A total of 40 patients over 60 years old were evaluated before treatment, and 2 months and 6 months after the beginning of treatment. Factor analysis isolated four factors of drug effect: 1) attention and concentration; 2) memory; 3) fluidity of conduct; and 4) manual activity. 12 references.

002092 Jus, Karolina; Jus, Andrzej; Beland, Claude; Bouchard, Marcel; Pires, Perpetua; Fontaine, Pierrette; Brunelle, Raymonde. Research Division, Hopital St-Michel-Archange, Quebec, Canada *Sleep analysis during drug-free weekends in chronic schizophrenic patients.* Biological Psychiatry. 11(6):709-718, 1976.

A polygraphic registration was made of the night sleep in a sample of 14 chronic schizophrenic patients who for several months (mean eight months) had been on a stable, relatively low maintenance dosage of neuroleptics administered according to the drug free weekend schedule (two consecutive drug free days at the weekend). During this treatment, their only complaint was of sleep deterioration during the drug free weekend nights, especially the second night. The polygraphic night sleep pattern of each patient was studied during two consecutive weeks. No difference was found between the adaptation night on medication and the consecutive night on medication during the first week, and between the adaptation and readaptation nights on medication during two consecutive weeks. There was no difference in any sleep parameters between the nights on medication and the first drug free nights. There was a significant difference in the total sleep time between the nights on medication and the second drug free nights. No difference was found in any other sleep parameters. The practical implication is, that to avoid any change in nocturnal behavior it is preferable to withdraw the medication on two nonconsecutive days in the week. The evaluation of both daily and nocturnal behavior seems to be a

useful tool in evaluating the first sign of the drug withdrawal syndrome. 20 references. (Author abstract modified)

002093 Kohnen, R.; Lienert, G. A. Regensburger Strasse 160, D-8500 Nuremberg, Germany /Free and questionnaire-controlled description of the effect of a hypnotic (flurazepam) by healthy subjects./ Freie und gebundene Wirkungsbeschreibung eines Schlafmittels (Flurazepam) durch gesunde Versuchspersonen. *Arzneimittel-Forschung* (Aulendorf). 26(6):1133-1136, 1976.

Questionnaire replies were compared with free descriptions of drug effects in an evaluation of 30mg flurazepam versus placebo. A group of 94 students were asked to describe how they fell asleep, how they slept and dreamt, and how they felt upon awakening and the following morning. They were instructed to compare the test night with normal sleep. The same parameters were covered in a questionnaire. In the free descriptions, five of the nine parameters significantly discriminated between flurazepam and placebo, whereas on the questionnaire, only one to nine items discriminated between the drug and placebo. There were more placebo reactors in the questionnaire method than in the free description method, but in the free description method, there were more noneffects to flurazepam. Flurazepam differed from placebo in that the subjects said they fell asleep faster, slept more deeply, and slept longer. 1 reference.

002094 Swahn, Carl-Gunnar; Sandgarde, Bengt; Wiesel, Frits-Axel; Sedvall, Goran. Division of Neuropsychopharmacology, Department of Pharmacology, Karolinska Institute, S-10401 Stockholm, Sweden Simultaneous determination of the three major monoamine metabolites in brain tissue and body fluids by a mass fragmentographic method. *Psychopharmacology* (Berlin). 48(2):147-152, 1976.

A mass fragmentographic method for the simultaneous determination of 4-hydroxy-3-methoxyphenylacetic acid (HVA), 4-hydroxy-3-methoxyphenylethylene glycol and 5-hydroxyindole-3-acetic acid was described. Deuterated analogues of the compounds were used as internal standards. The specificity was proved by multiple ion analysis. The experimental error was below 7% when applied to the analysis of human lumbar cerebrospinal fluid, urine, or rat brain tissue. In cerebrospinal fluid the major part of the monoamine metabolites occurred in the free form. In rat brain and human urine considerable amounts of conjugated HVA was found. 17 references. (Author abstract)

002095 Ulrich, G.; Harms, K.; Fleischhauer, J. Abteilung fur Psychophysiologie, Freie Universitat Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany /Investigations with a behavior oriented assessment scale for depressive inhibition and agitation: results of a video documented amitriptyline mianserine study./ Untersuchungen mit einer verhaltensorientierten Schatzskala fur depressive Hemmung und Agitation: Ergebnisse einer videodokumentierten Amitriptylin-Mianserin-Studie. *Arzneimittel-Forschung* (Aulendorf). 26(6):1117-1119, 1976.

A scale was developed for rating nonverbal behavior. Clinical material consisted of videotaped interviews with 20 depressed female patients involved in a comparison of amitriptyline and mianserine. Interviews were conducted before, and about 21 days after treatment began, and evaluated by two investigators. Two measures were computed: the G-index of Holley and Guilford and the transinformation quotient (TQ). Agitation and inhibition showed a TQ of 0.39. This new method helps show the role of nonverbal behavior in the process of making a diagnosis, and helps define the concepts used. 4 references.

002096 Wang, H. S.; Obrist, Walter D. Department of Psychiatry, Duke University Medical Center, Durham, NC Effect of oral papaverine on cerebral blood flow in normals: evaluation by the Xenon-133 inhalation method. *Biological Psychiatry*. 11(2):217-225, 1976.

Biological research was done to clarify some issues of the use of vasoactive drugs in the treatment of neuropsychiatric disorders secondary to cerebrovascular insufficiency. The use of a noninvasive cerebral bloodflow (CBF) method in evaluation of oral papaverine, a commonly used vasoactive drug, was explored. Series CBF measurements were made by the Xe133 inhalation method in 21 healthy young adults, using a double-blind crossover experimental design. The findings show that oral papaverine significantly increases blood flow under conditions of both normal breathing and hyperventilation, the latter being used to induce cerebral vasoconstriction. There were large variations in individual response to the drug, and the average increase in CBF (6 to 9%) was smaller than that observed by other investigators using intravenous papaverine. No adverse reactions or alterations in blood pressure were encountered. 25 references. (Author abstract modified)

17 MISCELLANEOUS

17 MISCELLANEOUS

002097 Ananth, J. Faculty of Medicine, McGill University, Montreal, Quebec, Canada **Treatment approaches to mania.** International Pharmacopsychiatry (Basel). 11(4):215-231, 1976.

Innovative approaches for the treatment of manic episodes in therapy resistant patients were studied. Included are those based on norepinephrine, dopamine, acetylcholine, serotonin, gamma-aminobutyric acid and permissive hypothesis, peripheral autonomic imbalance, endocrine abnormalities, electrolyte disturbances, paradoxical response, cyclic AMP, pyrotherapy and antidepressants. Varied pharmacological approaches may yield discrete groups which are clinically and biochemically distinct since different etiological factors may produce very similar clinical pictures. This unitary syndrome with different biochemical abnormalities implies that no single drug can improve all cases of mania. The various treatment modalities described provide guidelines for the clinician faced with the problem of treating a manic patient not responding to usual methods of treatment. 86 references. (Author abstract modified)

002098 Angst, J.; Baumann, U. Psychiatrische Universitätsklinik, Zurich, Switzerland /Methodology of clinical testing of antipsychotics./ Zur Methodik klinischer Prüfungen von Antipsychotika. Psychofarmakoterapia Schizofrenii Lekii o Przegluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat. Odd. Wroclawski, 1976. 256 p. (p. 59-72).

In a paper presented at a symposium on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, aspects of the methodology of clinical testing of antipsychotic drugs are discussed. Among the methods of evaluation discussed are: BPRS (Brief Psychiatric Rating Scale), electronic data processing, statistical evaluation of symptoms, and diagnostics (syndrome evaluation). The study indicates a need for a universal clinical evaluation system to facilitate quantitative comparative system evaluations. 9 references.

002099 Ayd, Frank J., Jr. Taylor Manor Hospital, Ellicott City, MD **Diagnosis in planning psychopharmacological therapy.** Bulletin of the Menninger Clinic. 40(5):541-548, 1976.

In a paper presented at a Scientific Conference held in October 1975 to honor the 50th anniversary of the Menninger Foundation, the notion that since the advent of potent psychopharmaceuticals, the task of the psychiatrist as diagnostician has decreased in importance was vigorously refuted, and an overview of the process of rational psychopharmacotherapy was presented. The use of psychopharmaceuticals requires that the physician prescriber be a skilled clinician, adept in history taking, and capable of making reasonably precise psychiatric diagnoses, including an assessment of the patient's basic personality. Furthermore, the physician prescriber must be knowledgeable about the patient's physical status, aware of his family and personal drug histories, and be acquainted with the clinical indications, contraindications, dosages, and pharmacological and toxicological properties of the various psychoactive drugs. Finally, since the physician prescriber is not simply treating an illness but a human being who has an illness, it is imperative he acknowledge that all patients require not just a drug but also compassion, understanding, and some degree of formal psychotherapy in order to achieve optimal therapeutic results.

002100 Ban, Thomas A. Div. of Psychopharmacology, Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Psychopathology, psychopharmacology and the organic brain syndromes: part II.** Psychosomatics. 17(3):131-137, 1976.

The three major therapeutic approaches in the pharmacological treatment of organic brain syndrome: symptomatic (by psychotropic drugs); palliative (by drugs with an effect on cerebral circulation); and causal (by substitution or replacement) are discussed. The uses of psychotropic drugs, hypnotics, anxiolytics, antipsychotics, stimulants and antidepressants for the treatment of symptoms often accompanying organic brain syndromes are examined. Anticoagulants and vasodilators have been used for the palliative treatment of organic brain syndromes based on the assumption that increasing the cerebral blood flow may help alleviate some of the psychopathological manifestations. Causal treatment may involve the administration of hormones, vitamins and ribonucleic acid (RNA) supplements or RNA stimulants such as magnesium pemoline. The role of pharmacological treatment in psychogeriatrics is briefly discussed. It has been suggested that geriatric pharmacotherapy should be based on electroencephalographic characterizations of the elderly patient. Research exploring the possible relationships between psychometric test performance responses to the psychopharmacological load and six different psychoactive drugs is presented. It was found that, of the six drugs investigated, thioridazine, nicotinic acid, and fluoxymesterone exhibited the greatest overall therapeutic efficacy in chronically hospitalized geriatric patients. 84 references.

002101 Barnhart, C. Clifton. Department of Psychiatry, University of Missouri Medical Center, Columbia, MO **LX — thirty-five years of psychosocial deprivation.** Psychiatric Opinion. 13(4):37-43, 1976.

A case history of a 39-year-old woman deprived of psychosocial contact for most of her life is discussed. It appeared that what this woman would respond to favorably was appropriate pharmacotherapy supplemented with abundant supportive measures geared toward resocialization. Months of progress, however, were negated by what was initially thought to be a rather inconsequential exposure to her old pathological relationship, suggesting the need to examine the influence and impact of this type of reexposure when reentry into society is a therapeutic goal.

002102 Barraclough, B. M. MRC Clinical Psychiatry Unit, Graylingwell Hospital, Chichester, West Sussex PO19 4PQ, England **Barbiturate prescribing: psychiatrists' views.** British Medical Journal (London). No. 6041:927-928, 1976.

A questionnaire on three aspects of barbiturate prescribing: 1) present prescribing habits; 2) therapeutic indications; and 3) legal restraints on prescribing, was mailed to a random sample of one in five consulting psychiatrists practicing adult psychiatry in England, Wales, and Scotland. Seventy percent replied that they never prescribed barbiturates for new patients, either for sleeplessness or for daytime sedation. Over 90% recommended chronic barbiturate takers to desist. Over 25% thought, however, that barbiturates were needed for treating sleeplessness, fewer for managing the anxious patient. Psychiatrists regard barbiturates with reserve as a treatment for sleeplessness or anxiety, excepting the unusual patient, but see a definite if limited place for barbiturates in the treatment of mental disease. 13 references.

002103 Bassuk, Ellen L.; Schoonover, Stephen C. Beth Israel Hospital, New York, NY *The practitioner's guide to psychoactive drugs*. New York, Plenum, 1976. 375 p. \$19.95.

A clinical overview of psychoactive drugs is presented for the clinician and researcher. Organization is by symptom presentation, and each psychotropic drug is discussed in terms of chemistry, side effects, toxicity, pharmacokinetics, preparation, and dosage. Topics covered include depression, clinical psychiatric disorders, psychosis, anxiety and insomnia, pediatric psychopharmacology, geriatrics, and drug abuse. Also included are descriptions of rarely indicated drug regimens and a comparison of alternative drug therapies. Characteristics, practical applications, and limitations of psychiatric drug therapy are emphasized. (Author abstract modified)

002104 Breathnach, C. S. Physiology Department, University College, Dublin, Ireland *Neurophysiology - Part IV*. Irish Medical Journal (Dublin). 69(13):353-355, 1976.

The transmission of information across a synapse is discussed in terms of chemical transmission vs. electrical transmission. Topics presented include: 1) acetylcholine and its role as a mediator at the motor endplate in skeletal muscle; 2) chemical transmission in the CNS by adrenaline (epinephrine), noradrenalin (norepinephrine), dopamine, serotonin (5-hydroxytryptamine), gamma-aminobutyric acid, glycine, and acetylcholine; and 3) receptors for these chemical transmitters within the CNS and peripheral nervous system, i.e., alpha-adrenergic receptors, beta-adrenergic receptors, nicotinic cholinergic receptors, and muscarinic cholinergic receptors. Some effects of drugs on these transmitters or on the receptors are briefly presented.

002105 Carey, Michael S.; Noyes, Robert W.; Pasquale, Samuel A.; Frey, John J.; Lawson, John S. Department of Medical Research and Statistics, Ortho Pharmaceutical Corporation, Route 202, Raritan, NJ 08869 *Developing optimum drug regimens*. Journal of International Medical Research (Northampton). 4(5):277-280, 1976.

In clinical pharmacological trials the determination of the optimum regimen for a drug using the technique of response surface analysis is proposed as being more advantageous than traditional analyses of dose response relationships. Major considerations in favor of this technique are that the optimum regimen can be identified with a minimum of human experimentation, and unacceptable regimens are eliminated from the study early, at a substantial saving of time and money. 6 references. (Author abstract)

002106 Castrogiovanni, P.; Cassano, G. B.; Conti, L.; Maggini, C.; Bonollo, L.; Sarteschi, P. Istituto di Psichiatria, Università di Pisa, I-56100 Pisa, Italy *An automated diagnostic process (PDA) in clinical psychopharmacology: an exemplification of its use in a sulpiride versus haloperidol comparative trial*. International Pharmacopsychiatry (Basel). 11(2):74-83, 1976.

To test the suitability of an automated diagnostic procedure (PDA) for multicenter drug trials, a double-blind comparative study of sulpiride vs haloperidol was carried out in 76 schizophrenic patients from 6 different psychiatric units. The diagnostic procedure gave a profile and diagnostic definition for each patient prior to the study, and provided data for the statistical analyses comparing the therapeutic efficacy of the two compounds after the treatment period. The agreement between clinician and computer diagnosis was 78.9%. Of the

patients for which there was clinician and computer diagnostic agreement, 69.2% sulpiride and 51.7% on haloperidol improved. The relationship of psychopathological patterns to drug responses is discussed. 8 references.

002107 Culpán, R. H. Department of Psychiatry, Auckland University School of Medicine, Auckland, New Zealand *The management of psychiatric emergencies*. Current Therapeutics (Milford). 17(9):41, 45, 47, 1976.

The effectiveness of pharmacotherapy in the treatment of psychiatric emergencies is considered in the absence of police action or mental hospital committal. Drugs, dosages and effects on dangerously aggressive patients, confused or restless patients, agitated or suicidal patients and anorexia nervosa which has reached the crisis stage are given. It is concluded that most psychiatric emergencies can be resolved through the use of drugs and that in the time gained diagnostic evaluations and the initiation or treatment can be effected without recourse to police intervention or certification.

002108 Czerniejewska, Maria; Moscirobrodowa, Bozena; Czerniejewski, Krystyn. Oddział Nerwicy Szpitala Miejskiego ZOZ, Oswiecim, Poland *Certain nonbiological aspects of the pharmacotherapy of schizophrenia./ Niektóre pozabiołogiczne aspekty farmakoterapii schizofrenii*. Psychofarmakoterapia Schizofrenii Lek o Przedłużonym Działaniu. Wrocław, Polskie Tow. Psychiat. Odd. Wrocławski, 1976. 256 p. (p. 53-57).

In a paper presented at a symposium on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wrocław, Poland, in October 1973, nonbiological aspects of the pharmacotherapy of schizophrenia, defined as the interaction of the patient with his environment, are examined. It is concluded that interaction with the environment can be highly beneficial in the application of drug therapy. Interaction which can provide a stimulus and response can later be utilized in evaluating the effectiveness of the drug being used. Interaction is strengthened by encouraging the patient to describe in detail his fears, emotions and state of well-being.

002109 Davis, Harry K. Department of Psychiatry, University of Texas Medical Branch, Galveston, TX 77550 *Updating Psychotropic drug therapy*. Texas Medicine. 72(9):39-47, 1976.

The use of major tranquilizers (neuroleptics, antipsychotics), minor tranquilizers (anxiolytic agents) and antidepressant drugs is discussed. The information included lists of drugs available in each category; dosage ranges; therapeutic uses; length of pharmacotherapy treatments; and factors to be considered in selecting a drug or changing to another drug. The need to take a complete drug history of the patient before prescribing and the hazards of polypharmacy (multiple drug therapy) are emphasized. Also discussed are the use of the unit dose concept, the practice of permitting patients to omit doses at specified intervals, and the complications and side effects associated with psychotropic drugs. Lithium carbonate and several new drugs are discussed individually. 20 references.

002110 Davis, John M. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, IL 60612 *Comparative doses and costs of antipsychotic medication*. Archives of General Psychiatry. 33(7):858-861, 1976.

Data derived from reviewing double-blind controlled studies that used a flexible dosage schedule of neuroleptics in treating schizophrenics is applied to the development of a table listing the equivalent dosage and comparative cost of the various an-

tipsychotic drugs, converted to 100mg chlorpromazine equivalents. This empirically derived dosage comparability table is compared with a similar table derived from the opinions of experts. In absolute amounts, the cost differences between drugs appears small. However, for any drug, large savings accrue when the largest possible capsule or tablet to achieve the desired dose is prescribed. 64 references. (Author abstract modified)

002111 Dawes, P.; Redfern, P. H. School of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, England A simple and inexpensive method for the intracerebral administration of drug solutions to the conscious rat. *British Journal of Pharmacology* (London). 58(3):464P, 1976.

A paper presented at the meeting of the British and French Pharmacological Societies (Sept. 1976) discussed a simple and inexpensive method for the intracerebral administration of drug solutions to the conscious rat. Stainless steel cannula guides cut to length dictated by topographical location of the brain area carries a small ball of epoxy resin which acts as guide anchorage and prevents movement in the vertical plane. Stilettes are of nonferrous wire coated with a water repelling agent and bent at the upper end over a length of polythene tubing secured by epoxy resin. This facilitates removal of the stilette from the guide and prevents access of foreign material. Guides are stereotactically positioned and secured to the surface of the cranium with polymethyl methacrylate. 2 references.

002112 Dement, W.; Holman, R. B.; Guilleminault, C. Stanford University School of Medicine, Stanford, CA 94305 Neurochemical and neuropharmacological foundations of the sleep disorders. *Psychopharmacology Communications*. 2(2):77-90, 1976.

A portion of the scientific literature dealing with the neurochemical mechanisms underlying sleep and waking is discussed and related to the clinical study and treatment of sleep disorders. The symptoms, characteristics and neuropharmacology of nocturnal myoclonus, narcolepsy and sleep apnea syndromes are presented. Findings of studies dealing with the drug therapy of the various sleep disorders are presented and some are discussed in terms of the biochemical mechanisms involved in the disorders. 65 references.

002113 Dray, A.; Straughan, d. w. Department of Pharmacology, School of Pharmacy, University of London, Brunswick Square, London WC1N 1AX, England Synaptic mechanisms in the substantia nigra. *Journal of Pharmacy and Pharmacology* (London). 28(4):400-405, 1976.

Research dealing with synaptic mechanisms in the substantia nigra (SN) is reviewed and discussed. Among the topics included are: 1) the morphology of the SN; 2) the content of putative transmitters in the SN; 3) the entrations of the transmitter; 4) the effects of the transmitters on single SN neurons; 5) the presence of drugs which have been shown to be antagonists of transmitters in the SN; 6) changes in SN transmitters occurring in disease states; and 7) physiological and pharmacological analysis of synaptic inputs into the SN. 55 references.

002114 Edvinsson, Lars; Owman, Christer; Sjöberg, Nils-Otto. Department of Histology, University of Lund, Lund, Sweden Autonomic nerves, mast cells, and amine receptors in human brain vessels. A histochemical and pharmacological study. *Brain Research* (Amsterdam). 115(3):377-393, 1976.

Histochemical and pharmacological studies were carried out on brain tissues obtained from 30 patients during lobe resection in conjunction with tumor surgery and from 17 fetuses obtained at legal abortions to obtain a more detailed knowledge about amine stores and receptor mechanisms in the cerebrovascular bed of man. Formaldehyde histofluorescence showed the presence of numerous perivascular adrenergic nerves around pial and intracerebral vessels, the carotid system being better supplied than the vertebral system. Cholinergic nerves, visualized by the cholinesterase technique, followed the adrenergic fibers in plexus formations of the pial arterial system. Histamine containing mast cells, often with a perivascular distribution, were located with the omicron-phthalaldehyde method. Transmural electrical stimulation of the perivascular nerves contracted isolated pieces of pial arteries in a frequency dependent manner, and the response was inhibited by the adrenergic nerve blocking agent, guanethidine. On the basis of the relative potency of various amines and related compounds in producing a motor response of isolated pial arteries, and the mode of inhibition caused by specific antagonists, various amine receptors could be demonstrated: adrenergic alpha-receptors (mediating contraction) and beta-receptors (dilation), cholinergic muscarinic receptors (dilation) and histamine H2 receptors (mediating dilation). Thus, the amine mechanisms demonstrated in human brain vessels appear to be principally the same as those shown in more extensive studies on laboratory animals. 51 references. (Author abstract modified)

002115 Ehrenpreis, Seymour; Kopin, Irwin J. Department of Pharmacology, Chicago Medical School, Chicago, IL *Reviews of neuroscience*. Vol. 2. New York, Raven, 1976. 277 p.

Six review articles on neurosciences are presented which address the following topics: 1) the blood/brain barrier as a regulatory mechanism; 2) possible mechanisms and biological significance of the variable sensitivity of excitable cells; 3) the synaptic transmitters involved in the release of hypothalamic releasing and inhibiting hormones; 4) endocrine and central nervous system effects of hypothalamic peptides and melanocyte stimulating hormones; 5) control in the development of the vertebrate sympathetic nervous system; and 6) the development of neurotransmitters and their function in the brain. A subject index is included. 1416 references.

002116 Engelhardt, David M.; Rosen, Bernard. Dept. of Psychiatry, State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203 Implications of drug treatment for the social rehabilitation of schizophrenic patients. *Schizophrenia Bulletin*. 2(3):454-462, 1976.

The implications of drug treatment for social rehabilitation of schizophrenic patients are examined. A long-term study of 541 schizophrenic outpatients revealed that phenothiazine treatment was effective in reducing the incidence of hospitalization, as well as delaying its occurrence among low competence, hospitalization prone patients. However, among high competence, nonhospitalization prone patients the hospitalization rate of patients receiving phenothiazine was not significantly different from the rate of those treated with placebo. It is noted that the effect of drug therapy on vocational rehabilitation remains unclear. Studies have revealed that while drug treatment is important in controlling symptomatology and maintaining the patient in the community, pharmacotherapy, by definition, cannot provide the patient with the motivation, skills, and opportunities necessary to obtaining and maintaining employment. When the schizophrenic patient

is supplied with an appropriate setting and support, his community functioning can be materially improved. It is concluded that the role of drug therapy in the social rehabilitation of schizophrenics needs further research to establish the extent to which pharmacotherapy enhances the schizophrenic patient's work performance in terms of greater stability, quality of performance, and upward mobility in the labor market. 49 references.

002117 Enzi, G.; Baritussio, A.; Marchiori, E.; Crepaldi, G. Department of Internal Medicine, University of Padua, Padua, Italy Short-term and long-term clinical evaluation of a non-amphetaminic anorexiant (mazindol) in the treatment of obesity. *Journal of International Medical Research* (Northampton). 4(5):305-318, 1976.

The effectiveness and tolerance of a nonamphetaminic anorexiant drug, mazindol, was evaluated in a short-term and in a long-term clinical trial in simple obesity and in refractory obesity. In the short-term crossover trial, a more evident effectiveness and tolerance result when the anorexiant is given in a late phase of treatment. The association of an anorexiant drug with the hypocaloric diet was seen to be effective in the treatment of so-called refractory obesity. In the evaluation of the long-term treatment it is seen that weight loss is greater and remains so for longer periods in patients receiving anorexiant, as compared to controls. This is related to a better maintenance of a restricted calorie regimen. Mazindol did not affect the improvement of glucose tolerance and insulin secretion which follows the weight reduction. 20 references. (Author abstract)

002118 Feldman, Harold S. Department of Psychiatry, New Jersey Medical School, Newark, NJ Psychopharmacology and the law: a forensic psychiatrist's viewpoint. *Journal of Clinical Pharmacology*. 16(10):577-580, 1976.

The formulation of a forensic psychiatric viewpoint relating to the law which must consider and summarize the pharmacology and therapeutics of psychoactive drugs used to treat patients is considered. Among the topics discussed are: 1) the conditions under which a mentally incompetent criminal offender may and should be brought to trial after drug therapy and/or during maintenance therapy with normalizing drugs; 2) three judicial decisions which secure for the committed mental patient the right to treatment; and 3) the associations between drug use and crime. The types of crime associated with use of alcohol, barbiturates, amphetamines, cocaine, marihuana, opiates, nonbarbiturate sedative/hypnotics and hallucinogens are discussed. 5 references.

002119 Ferris, Gilbert N. 3415 Floyd Ave., Richmond, VA 23221 Psychotropic drugs in opioid addicts on methadone treatment. *Diseases of the Nervous System*. 37(7):400-403, 1976.

Psychotropic drug treatment of drug addicts on methadone maintenance is discussed and four case histories are used as examples. Patients with clear target symptoms, such as anxiety, depression, or psychosis responded just as nonopioid addicts would to the major psychotropic agents. The minor tranquilizers are felt to be of doubtful value, and subject to abuse. Sleep disturbances cannot be treated by the usual means, as the drugs needed again are abused; however, chlorpromazine shows some promise here. Methods of drug delivery and goals of treatment must be adapted to the realities of this patient group's characteristics, particularly antisocial traits, poor motivation and unreliability. Psychotropic drugs are unlikely to be of aid in multiple drug abusers, personality and character disorders, and opioid withdrawal. 8 references. (Author abstract)

002120 Gottschalk, Louis A.; Merlis, Sidney. no address Pharmacokinetics of psychoactive drugs: blood levels and clinical response. New York, Spectrum Publications, 1976. 268 p. \$20.00.

Papers dealing with methodological problems and approaches in studying the pharmacokinetics of psychoactive drugs and with the pharmacological/clinical relationships of psychoactive drugs are presented.

002121 Grahame-Smith, D. G. University of Oxford, MRC Unit of Clinical Pharmacology, Oxford, England Drugs which alter the mind. *Nursing Times* (London). 72(48):1881-1883, 1976.

Present and future trends in the use of psychotropic drugs are discussed. The medical profession has found itself in a position of prescribing mind altering drugs, almost on demand, for a host of minor psychological problems. The drugs are taken eagerly, with little consideration of their neurophysiological action in the brain, varying effects on individuals, or the possible long-term effects of chronic administration. That more powerful psychopharmacological agents will be discovered is inevitable. It is urged that society be educated about this prospect and its implications if we are to avoid the state of affairs outlined in Huxley's *Brave new world*, where drugs are desired, and available, to avoid every unpleasant state. 5 references.

002122 Groves, Philip M.; Rebec, George V. Department of Psychology, University of Colorado, Boulder, CO 80302 Biochemistry and behavior: some central actions of amphetamine and antipsychotic drugs. *Annual Review of Psychology*. 27:91-111, 1976.

An overview of current research on the biochemical, neurophysiological and behavioral correlates of amphetamine administration is presented. Studies reviewed concern neurotransmitters released by amphetamine, amphetamine effects on neurotransmitter inactivation and on the regulation of monoamine biosynthesis, amphetamine induced locomotor and stereotyped behavior, the role of central neurotransmitters in the behavioral effects of amphetamine, damage to the nigro neostriatal system prior to amphetamine administration and correlates of long-term amphetamine administration. It is felt that one of the most impressive aspects of current research on the mechanisms of action of amphetamine and related antipsychotic drugs is the close similarity between amphetamine psychosis and paranoid schizophrenia. 383 references.

002123 Gruchow, H. William. Health Studies Programme, University of Waterloo, Waterloo, Ontario, Canada Catecholamine activity and reported morbidity. *Journal of Chronic Diseases* (Oxford). 29(12):773-783, 1976.

Urinary vanillylmandelic acid (VMA) levels were measured in relation to the reporting of morbidity in an attempt to determine whether altered catecholamine activity is related to specific disease syndromes, or is a general characteristic of morbidity. The cross-sectional data show elevated VMA levels to be associated with the reporting of chronic disease conditions; nonchronic conditions and affective disorders were associated with lower VMA values. Although these findings are interpreted as supporting the hypothesis that psychosocial stimuli acting through the sympathetic adrenal medullary system may be important in the etiology of chronic disease conditions, alternative explanations are discussed and the need for further longitudinal studies indicated. 39 references. (Author abstract)

002124 Hesbacher, Peter; Rickels, Karl; Rial, William Y.; Segal, Asher; Zamostien, Bernard B. Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19174 **Psychotropic drug prescription in family practice.** *Comprehensive Psychiatry*. 17(5):607-615, 1976.

Direct psychiatric assessment of outpatients with emotional problems in seven family practices were conducted in order to assess the relationship of present psychiatric status to current and prior treatment with pharmacotherapy, and to describe the utilization of psychotropic drugs by type and frequency. The types of psychotropic drugs prescribed in family practice included antianxiety agents, antipsychotics, antidepressants, sedatives, and stimulants. It was determined that family physicians choose from a limited range of medications, generally utilizing those regarded as most effective, and are judicious in their choice of patients to treat in this manner. 19 references.

002125 Holden, Constance. no address **Amphetamines: tighter controls on the horizon.** *Science*. 194(4269):1027-1028, 1976.

Results of hearings held by Senator Gaylord Nelson in November, 1976, on the safety and efficacy of antiobesity drugs are summarized; it is noted that amphetamine abuse is still a major problem, and that amphetamines are widely available in spite of strict federal controls on the manufacture and distribution of such drugs since 1971. Although prescriptions of amphetamines have been reduced, consumption of amphetamine like drugs had gone up, and it is suggested that these drugs should be outlawed for use in combating obesity. Practices of companies which manufacture in foreign countries when manufacture is restricted in the United States are described. Most amphetamines and amphetamine like drugs are obtained legally; the American Medical Association has made little attempt to curb the problem. It is concluded that technological approach to solving human problems is represented by treating obesity as a disease rather than a condition, thus making it acceptable to prescribe an antiobesity pill.

002126 Iveson-Iveson, Joan. Surrey House, 1 Throwley Way, Sutton, Surrey SMI 4QQ, England **Haloperidol: a useful psychiatric drug.** *Nursing Mirror and Midwives Journal* (London). 143(20):77, 1976.

Psychiatric uses of haloperidol are discussed. First synthesized in 1958, it has been proven extremely successful in the treatment of hypomania, mania, and acute and chronic schizophrenia, as well as for the treatment of alcohol withdrawal, child behavioral disorders, and Gilles de la Tourette syndrome. It is available in liquid or tablet form and has been proven more potent, and with fewer sedative effects or autonomic side-effects, than many of the phenothiazines. Its relative safety, speed of action and potential for permitting the earlier release of many psychiatric patients make it a drug with which psychiatric nursing staffs will have to familiarize themselves. 1 reference.

002127 Jayaratna, P. S.; Gottlieb, B. St. Stephen's Hospital, London SW10 9TH, England **Hypothyroidism with episodic psychiatric and cardiac manifestations.** *Proceedings of the Royal Society of Medicine* (London). 69(8):581-582, 1976.

The case of a 61-year-old woman with a history of rheumatic fever, depression, mental confusion and disorientation (diagnosed as hypomania) and coma is discussed. Periods of psychiatric symptoms were accompanied by ECG changes. Hypothyroidism was later diagnosed, and treatment with thyroxine relieved both psychiatric and cardiac symptoms. Brief discussion of the case follows. 4 references.

002128 Johnson, F. N. Department of Psychology, University of Lancaster, Lancaster, Lancashire, England **On the relevance of animal studies on lithium to the understanding of lithium therapy.** *Comprehensive Psychiatry*. 17(5):591-599, 1976.

A discussion of why lithium has not been sufficiently examined under controlled laboratory conditions is presented. Numerous questions are posed and examined: 1) why so long a delay occurred before animal behavior studies commenced; 2) why animal behavior studies have not been pursued vigorously; and 3) why practically no change in the conceptualization of lithium therapy has been apparent despite arguments in early publications on the psychopharmacology of lithium salts that behavioral effects of lithium ions must inevitably change the way in which lithium therapy, and possibly the affective disorders themselves, had to be conceptualized. It is concluded that behavioral work with lithium is subject to serious limitations insofar as it is possible to set up experimental analogues of the clinical treatment situation and that there is an important role for such work. 22 references.

002129 Johnson, G. F. S. Department of Psychiatry, University of Sydney, Royal Prince Alfred Hospital, Camperdown, NSW 2050, Australia **Clinical use of antidepressant drugs.** *Current Therapeutics* (Milford). 17(10):33-41, 1976.

The treatment of depression with tricyclic antidepressants, monoamine oxidase inhibitors (MAOI), or lithium carbonate (Li) is reviewed. Antidepressant drugs should be used in cases of acute depressive syndrome or recurrent depression. The need for psychological treatment, alone or in combination with drug therapy in some cases, is discussed. The tricyclics are the drugs of choice; MAOIs are indicated only for treatment resistant depression because of their variable efficacy and major potential for side-effects. Li is not indicated for the treatment of acute depression, but Li or the tricyclics are effective in preventing recurrences of depressive illness. Patients who have had an episode of hypomania or mania should be treated with Li. The mechanism of action and adverse effects of the tricyclics and MAOIs are discussed. The onset of clinical response to the tricyclics is 7 to 21 days; therefore, an adequate trial requires at least 3 weeks. Due to the marked differences in individual rates of metabolism, dosage regimens must be individualized. The optimal dosage should be maintained until clinical remission occurs. A reduced dosage is recommended for 3 to 6 months, followed by a gradual withdrawal. It is unlikely that a patient unresponsive to one tricyclic will respond to another. Patients on maintenance treatment should be reviewed regularly to assess the clinical response and evidence of adverse reactions. With Li therapy, pretreatment laboratory studies of renal and thyroid function and regular serum level determinations are mandatory. 4 references.

002130 Kety, Seymour S. Harvard Medical School, Boston, MA **Lithic substrates of mental illness.** *Western Journal of Medicine*. 125(6):491-493, 1976.

Advancement in the neurobiological sciences and in understanding of drugs used to treat mental disorders is discussed. It is noted that although the "antipsychiatry" movement opposes the medical model of mental illness, that model and the sciences upon which it depends have made progress in the treatment of mental illness, and have elucidated some of the neurobiological processes on which an understanding of their causes and pathogenesis may well depend. The use of drugs in the treatment of such disorders as schizophrenia, depression, and mania is discussed. It is men-

tioned that heredity and familial studies show genetic factors in mental illness, which indicates that biochemical processes play a significant role in these disorders. The discovery of the chemical nature of the brain synapse is mentioned as an important contribution to neurobiological research. It is suggested that such research may be used to advance understanding of the neurobiological components of mental illness. 5 references.

002131 Keyserlingk, Hugo von. Sonnenbergstr. 1a, DDR-6900 Jena, Germany /*One hundred fifty years of psychiatric therapy./ 150 Jahre psychiatrische Therapie. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig).* 28(6):321-333, 1976.

The history of psychiatric treatment during the past 150 years is reviewed. The early period was marked by gradual segregation of mental patients from common criminals and the lessening of physical restraints at mental asylums. Morphine, opium, and other sedatives were introduced in the decades after 1850. The turn of the century saw improvements in the quality of care, the employment of psychiatric nurses, and domestic activity for mildly disturbed patients. The efficacy of fever treatments was debated. Rehabilitation of patients through "active therapy" became more accepted in the 1920's. The continued care of discharged patients, partly through volunteer organizations, became feasible in the same decade. Insulin therapy was first administered to patients who refused food; the quieting effects of the drug were subsequently observed in psychotics. Drug induced convulsions were complemented by electric shock therapy where indicated. The psychopharmacological era began in 1952 with the introduction of chlorpromazine. As a result of drug treatment, patients were discharged early and were supported by day or night clinics. In the future, large psychiatric hospitals may be replaced by decentralized facilities. Personnel presently classified as paraprofessionals will play an important role in future psychiatric care, as they do now in the Soviet Union. As past experience has shown, psychiatry will solve its most pressing problem, that of endogenous psychoses, only with the methods of natural science. 74 references.

002132 Kornetsky, Conan. no address /*Pharmacology: drugs affecting behavior.* New York, John Wiley, 1976. 275 p. \$18.95.

The physiological and psychological effects of drugs often used with the mentally ill, with epileptics, with hyperactive children, and by drug abusers are introduced and explained. Topics covered include the vocabulary of pharmacology; explanation of the basic mechanisms governing the autonomic and central nervous systems; descriptions of antipsychotics, antidepressives, narcotic analgesics, hypnotics and sedatives, alcohol, amphetamines, and antiepileptic drugs; illicit drug use; and a glossary of street drug terms. Coverage on hyperactive children reviews much of the current knowledge about the syndrome and its pharmacology. (Author abstract modified)

002133 Lacoursiere, Roy B.; Spohn, Herbert E. Chemical Problem Treatment Program, Veterans Administration Hospital, Topeka, KS 66622 /*How long does chlorpromazine last? Journal of Nervous and Mental Disease.* 163(4):267-275, 1976.

The data on persistence of chlorpromazine in chronically medicated schizophrenic patients after drug discontinuation was reviewed to clarify previous indications of persistence from a few to several days in blood and up to many months in urine; clinical data also indicate long-term therapeutic effects. At least two implications of the question were considered: 1) the pharmacological persistence of an active drug and/or

metabolites after drug discontinuation; and 2) the persistence of the therapeutic effects regardless of whether or not an active drug and/or metabolites are pharmacologically present. This examination of the literature demonstrates a duration of substantial pharmacological (therapeutic) action of chlorpromazine of no more than a few days after drug discontinuation. For a small number of patients, clinical deterioration begins about the same time, whereas in many others, clinical improvement lasts weeks or months. Some of this latter continuation of improvement is probably not due to currently active chlorpromazine and/or metabolites. Many unanswered questions remain regarding the persistence of minute amounts of chlorpromazine and/or metabolites in storage and possibly at active sites, and whether or not in some patients this makes a significant contribution. 46 references. (Author abstract modified)

002134 Lambert, P.-A.; de Maximy, B. Clinique de Bressieux, Hôpital de Bassens, F-73011 Chambéry, France /*Anxiety and depression: differential diagnosis and treatment in daily practice./ Anxiété et dépression. Diagnostic différentiel et traitement en pratique quotidienne. Semaine des Hôpitaux: Thérapeutique (Paris).* 52(9):501-503, 1976.

Characteristics of anxiety and depression are given in order to enable the nonpsychiatric practitioner to distinguish between the two states. Anxiety and depression can also occur together. For anxiety, clobazam is recommended, and a tricyclic drug is recommended for depression.

002135 Lasagna, Louis. Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 /*Professional disagreement in drug efficacy study./ Consensus among experts: the unholy grail. Perspectives in Biology and Medicine.* 19(4):537-548, 1976.

An essay discusses the professional disagreement in response to a drug questionnaire administered to five clinical pharmacologists, five medical internists and six experts from a National Academy of Science Drug Efficacy Study panel concerning the use of Ritalin (methylphenidate), Equagesic, Chloromycetin (chloramphenicol), B-12 injection and oral contraceptives. Respondents were asked to approve or disapprove on a five point scale a product's use for specific reasons and diagnostic groups. The areas of disagreement and agreement are outlined, and the preponderance of disagreement is cited as reason for curtailment of the increasing regulatory measures in this area and adoption of a more pluralistic approach. 1 reference.

002136 Le Gall, Andre. Societe internationale d'etude de la Personnalité et du Caractère /*Characterological significance of medication./ Signification caractérolologique du médicament. Caractérolologie (Paris).* No. 19:63-70, 1976.

The importance and value placed on medication by both the doctor and the patient is as crucial to its effectiveness to a patient as is its therapeutic power. Pharmacological research concerning serious side-effects of drugs is needed. Some doctors and patients appear more impressed with the novelty and high cost of a new drug than its therapeutic value where others want only well tested medication. Educational information for both doctors and patients on the value of medication is needed. Periodically the public is alerted to the ineffectiveness and proliferation of useless pharmaceuticals. It is cautioned that the use of tranquilizers to relieve physical manifestations of inner anxiety only relieves symptoms but does not remove the cause of anxiety.

002137 Leeds, Alice A. International Reference Center for Information on Psychotropic Drugs, NIMH, 5600 Fishers Lane, Rockville, MD 20857 /The International Reference Center for Information on Psychotropic Drugs of the World Health Organization. (Summary)./ Das internationale Referenzzentren-System der Weltgesundheitsorganisation für die Information über Psychopharmaka. (Kurzfassung). Arzneimittel-Forschung (Aulendorf). 26(6):1024-1025, 1976.

The International Reference Center of the World Health Organization (WHO) for Information on Psychotropic Drugs is described. There are 25 nations participating. The Center keeps psychopharmacologists informed of the newest research in the field. The data on new psychotropic drugs collected includes identification of the drug, chemical structure and formula, type of drug (e.g., major tranquilizer, antidepressant, etc.), LD-50, dosage in animals and humans, indications and contraindications, side-effects, and results of studies. The information is duplicated and sent to information centers in participating countries. In addition, the Center keeps a file of names and addresses of 2100 psychopharmacologists in 54 countries. It distributes the Psychopharmacology Bulletin in 143 countries. Abstracts of special articles from the world literature can be sent out usually within a week.

002138 Levine, Jerome. Psychopharmacology Research Branch, NIMH, 5600 Fishers Lane, Rockville, MD 20857 In the service of psychopharmacology research: the PSC-PRB, NIMH Program 1956-1976. (Unpublished paper). Rockville, MD, NIMH, 1976. 7 p.

The first twenty years of operation of the Psychopharmacology Service Center/Psychopharmacology Research Branch (PSC/PRB) of NIMH, detailing its establishment, functioning, and governmental relations are described. The cooperation between the PSC/PRB and the ACN is described as synergistic. The PSC/PRB has been the principal federal source of support for research in psychopharmacology: preclinical or clinical, basic or applied. Substantive goals are: 1) to increase knowledge of the ways by which drugs influence thought, mood, and behavior; 2) to stimulate and assess the pharmacologic treatment of mental disorders through the support and conduct of clinical trials; 3) to assess the extent and character of legitimate psychotropic drug use and its impact on society; and 4) to disseminate information so as to foster research on, and increase the usefulness of, the pharmacotherapy of mental disorders. 4 references.

002139 Levine, Jerome. Psychopharmacology Research Branch, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20857 Psychotropic drug assessment -- current status, future prospects. (Unpublished paper) Washington, DC, NIMH, 1976. 14 p.

The scientific methodology and administrative processes through which chemicals with potential psychotherapeutic value become marketed drugs for the treatment of psychiatric disorders are reviewed and discussed. Judgments as to future prospects, including the expectation that clinical methodology will be improved, are also presented. 9 references.

002140 Levitt, R. A. no address Psychopharmacology -- a biological approach. Washington DC, Hemisphere, 1975. 502 p. L9.45.

An overview of psychopharmacology integrating physiological, pharmacological and behavioral information is presented. General pharmacological principles are discussed. Biochemical neuropharmacology is covered including information on synap-

tic transmission. Centrally acting drugs are described including stimulants, depressants, antischizophrenic drugs and hallucinogenic drugs. Chapters on learning, memory, behavioral endocrinology and sexual behavior are also included. (Author abstract)

002141 Lewandowski, G. Bundesgesundheitsamt, Thielallee 88-92, D-1000 Berlin 33, Germany /The new drug statute and the future of clinical psychopharmacology./ Das neue Arzneimittelgesetz und die Zukunft der klinischen Psychopharmakologie. Arzneimittel-Forschung (Aulendorf). 26(6):1022-1024, 1976.

A new drug act being considered by the parliament of the Federal Republic of Germany and its effect on the practice of clinical psychopharmacology are discussed. The legislation would affect clinical drug trials. It is concluded that the new drug act would protect the interests of patients without seriously affecting the clinical research that is necessary for progress in therapeutics. 23 references.

002142 Mandel, S. P. H.; Levine, A.; Beleno, G. E. Biometrics Unit, Dept. of Mathematics, University of Otago, Dunedin, New Zealand Signalling increases in reporting in international monitoring of adverse reactions to therapeutic drugs. Methods of Information in Medicine (Stuttgart). 15(1):1-10, 1976.

The present state of international monitoring of adverse reactions to therapeutic drugs based on spontaneous, voluntary, haphazard reporting is reviewed. A number of different avenues of research could be usefully pursued to provide signals for increases in reporting which are more specific and more sensitive than those currently available. In particular, the center batch matrix is introduced, and it is shown that the information it contains can be used to provide signals which are more informative than those obtained from data aggregated over several reporting centers. Other approaches introduced include methods for the detection of patterns of adverse events, the use of system measures for monitoring the monitoring system itself, and the potentialities of signals based on quantitative data. 21 references. (Author abstract modified)

002143 Mann, Henry B.; Greenspan, Stanley I. 54 Liberty St., Madison, CT 06443 The identification and treatment of adult brain dysfunction. American Journal of Psychiatry. 133(9):1013-1017, 1976.

It is hypothesized that adults who have had minimal brain dysfunction as children constitute a distinct diagnostic entity since adult brain dysfunction (ABD) may exist alone or with a variety of other psychiatric syndromes. Patients with ABD share a basic impairment in ability to focus attention effectively but may have different personality structures, symptom complexes, and behavioral patterns. Two case studies are provided to illustrate the hypothesis. Medical and psychotherapeutic treatment which may consist of antidepressants, stimulants, and psychotherapy can correct the impairment and improvement can be noted in both personality structure and behavior. 15 references. (Journal abstract modified)

002144 Marriott, Peter. 72 Roberts Street, Essendon, Vic. 3040, Australia Tranquilizers in general practice. Medical Journal of Australia (Glebe). 1(20):765, 1976.

In a letter to the editor, commentary on the use of alternative drugs to the benzodiazepines in the treatment of anxiety is offered. Flexible dosage based on age, sex and genetic makeup is suggested. Use of haloperidol and consequent side-effects

such as acute dystonia in young males, long-term use of the butyrophenones, dosage of diazepam and danger of combination of the above mentioned drugs with barbituates are briefly discussed. 2 references.

002145 Martinez Pina, A.; Irache, E.; Pardell, H. no address /Methodological review of fluid-therapy in psychiatry./ Revision metodologica de la fluidoterapia en psiquiatria. Rev. de Psiquiatria y Psicologia Med. de Europa y America Lat. (Barcelona). 12(7):413-428, 1976.

A study of revised methodology with antidepressive fluid therapy is presented and the results are compared with six previous studies. The subjects selected were 96 patients who had responded negatively to oral medication. Improvement was noticed about the 8th day and maximum improvement by the 13th day. Average length of intravenous treatment was 22.8 days. Four parameters were considered when determining treatment: course of the illness, psychopathological profile, social and family circumstances, and type of oral drug previously used. Considerations of these variables permitted successful use of fluid therapy when a variety of symptoms were present including insomnia, suicidal ideation, anxious depression, as well as gynecological, digestive, cardiopulmonary, and cephalalgic syndromes. 27 references.

002146 Nadel, Alan M.; Wilson, W. P. 1314 Peabody Ave., Memphis, TN 38104 Dialysis encephalopathy: a possible seizure disorder. Neurology. 26(12):1130-1134, 1976.

Dialysis encephalopathy is a progressive, fatal condition that occurs in patients receiving hemodialysis. It is characterized by abnormalities in speech, myoclonic jerks, and striking changes on the electroencephalogram. Dramatic reversal of the clinical symptoms and EEG abnormalities in four patients with this syndrome who were treated with diazepam was observed. It is proposed that in dialysis encephalopathy, some of the symptoms and the electroencephalographic changes represent a form of seizure disorder. 28 references. (Journal abstract modified)

002147 National Library of Medicine. National Library of Medicine, National Institutes of Health, Bethesda, MD Psychopharmacology -- a recurring bibliography. Psychopharmacology Bulletin. 12(3):S1-S56, A57-A96, 1976.

An extensive bibliography, indexed by subject and author, is presented of recent papers on psychopharmacology from the international scientific community. In 249 subject fields, 2832 citations are given.

002148 no author. no address New tranquilizer labels stir maternal anxiety. Medical World News. 17(18):20, 1976.

Reaction by pregnant women and pharmaceutical companies to FDA required warnings regarding the use of meprobamate, diazepam, and chlorthalidopoxide in the first trimester and associated increase of risk of congenital malformations are discussed. The warning is based on three methodologically different studies conducted at the University of California, Boston University (using data from the National Institute of Neurological Disease and Stroke), and the Center for Disease Control. Additional data was provided by an English study which analyzed the Finnish Register of Congenital Malformations. Although the warning is considered mild, the anxiety of pregnant women in considering the effects of such drugs on the fetus is high.

002149 no author. no address /The psychiatry of systemic lupus erythematosus./ The psychiatry of SLE. Practitioner (London). 217(1297):13, 1976.

Four cases pointing to the possibility of cerebral involvement as a feature of systemic lupus erythematosus are briefly presented. In all four cases symptoms of mental disorder such as memory impairment, disorientation, depression and hallucination were alleviated by the administration of prednisolone. Reduction or discontinuation of prednisolone seemed to cause an increase in mental disorders. It is suggested that a closer look at patients in psychiatric institutions might reveal previously undiagnosed and potentially treatable cases of SLE.

002150 no author. no address Drugs requested by defendant did not impair ability to stand trial. United States v. Hatrack, 408 F.Supp. 476. U.S. District Court. D. New Jersey. February 19, 1976. Mental Health Court Digest. 20(6):5, 1976.

In a 1976 habeas corpus proceeding by a New Jersey state prisoner, the U.S. District Court found that drugs received by the defendant at his own request did not render him incompetent to stand trial; did not impair his demeanor before the jury; and did not prevent him from receiving a fair trial. Counsel and psychiatric reports concurred that the prisoner was in fact competent to stand trial. (Journal abstract modified)

002151 no author. no address The introduction of chlorpromazine. Hospital & Community Psychiatry. 27(7):505, 1976.

The development of chlorpromazine is briefly reviewed, and its impact on mental health care in America is suggested. The general use of chlorpromazine and reserpine by many mental hospitals has led to declines in resident patient populations and a revolution in the care of psychiatric patients. 1 reference.

002152 no author. no address Use of tranquilizer insufficient to show lack of competency for trial. United States v. Smith, 521 F.2d 374 (Kansas). U.S. Court of Appeals. Tenth Circuit. August 22, 1975. Mental Health Court Digest. 19(11):3, 1976.

In a 1975 proceeding affirming conviction of voluntary manslaughter, the U.S. Court of Appeals found that, ignoring the self-administered aspect of the matter, the record did not show that the appellant's use of Valium, per se, rendered him incompetent during trial. (Journal abstract modified)

002153 Patzold, U.; Kruger, H.; Angermeyer, M. Neurologische Klinik der Medizinischen Hochschule, Postfach 610180, D-3000 Hannover 61, Germany /Influence of nonpharmacological factors on administration of neuroleptics in the stationary treatment of acute psychiatric conditions./ Einfluss nicht-pharmakologischer Faktoren auf den Neuroleptikaverbrauch bei stationar-psychiatrischer Akutbehandlung. Psychiatrische Praxis (Stuttgart). 3(4):222-229, 1976.

The effect of nonpharmacological factors on the efficacy of neuroleptic drugs was investigated. Patients with endogenous psychoses (excluding depressives) at two institutions were compared in their consumption of low potency and high potency neuroleptics. Patients admitted to a university hospital's psychiatric ward received doses approximately 2.5 times higher than patients of a municipal psychiatric clinic. The choice of high potency drugs was also more pronounced at the medical school. It is suspected that the explanation for dissimilar therapeutic methods can be found in divergent organizational structures and personality traits of physicians which affect interaction with patients. The medical school permitted relatively unrestricted circulation of patients, with harmful consequences for the psychological atmosphere. Due to a shortage of beds,

patients of both sexes at times shared perfunctorily screened sleeping areas. Attending personnel at the medical school averaged 25.3 years of age, compared to 37.3 years at the city hospital. The university psychiatric ward also experienced a turbulent turnover of physicians, therapists, and social workers. 15 references.

002154 Pavesi, Vittorio. Ente Ospedaliero Ronzoni-Principessa Jolanda, Milan, Italy /Prescription of an antidepressant and the physician-patient relationship./ La prescrizione di un antidepressivo nel rapporto medico-paziente. *Medicina Psicomatica* (Roma). 21(2):153-159, 1976.

Prescription of antidepressant drugs and their effects upon the physician-patient relationship are evaluated. Noxityline, selected as a typical drug, was administered to 20 patients. The drug, the patient, and the physician and their interrelationships are discussed. It is suggested that in order for a drug indication to be correct, the patient must communicate his problems to the physician. Correct prescription is based on critical valuation by the physician, and this can occur only through appropriate doctor-patient rapport. Unfortunately, lack of correct training on the part of the physician has resulted in incorrect diagnosis of the patient's problems, with resultant incorrect prescription. It is concluded that only with psychological training can the physician become aware of this serious problem in the doctor-patient relationship. 3 references.

002155 Pervomayskiy, B. Ya. no address /Current problems of psychiatric nosology./ Ob aktual'nykh voprosakh psikhicheskoy nozologii. 76(5):777-780, 1976. *Zhurnal Nevropatologii i Psikhatrii imeni S.S. Korsakova* (Moskva).

The problem of nosology in psychiatry as opposed to Neyman's concept of a single psychosis is explored. It is stated that some psychiatrists incorrectly see the difference between psychosis and neurosis as one of degree, while the transition from the former to the latter should be regarded nosologically. Neyman's concept of a single psychosis is labeled antiquated and incorrect and the importance of Pavlov's work is stressed. Nosology aids psychopharmacology in supplanting standard doses for all mental illnesses with precise doses tailored to the disorder. 10 references.

002156 Platman, Stanley R.; Dorgan, Richard; Gerhard, Ronald J. no address *Psychiatric medication: the role of the non-physician*. *International Journal of Social Psychiatry* (London). 22(1):56-60, 1976.

The functional role of 33 nonphysicians affiliated with a psychiatric center which has been delivering direct services to a segment of a large metropolitan area for 18 months is discussed. All direct services have been outcare delivered by nonphysician staff, utilizing physicians for consultation, supervision, and specific medical purposes. Each nonphysician staff member has clinical responsibility for his entire caseload of patients. He is expected to treat, inform, refer, and create linkages to other community resources. Treatment may consist of counseling, group treatment, rehabilitation, and medication. Over 75% of the 667 outcare patients receive one or more medications. These nonmedical service providers are expected to initiate, maintain and terminate prescription of medications. The staff member completes the prescription and directly delivers the medication. A physician signs each prescription, and thus provides quality control by setting upper and lower limits on dosages. The preliminary data from the study suggests that the prescribing of psychiatric medications is within the competence of nurses, social workers and psychologists. 3 references. (Author abstract modified)

002157 Quitkin, Frederic; Rifkin, Arthur; Klein, Donald F.; Davis, John M. no address *On prophylaxis in unipolar affective disorder*. *American Journal of Psychiatry*. 133(9):1091-1092, 1976.

A letter to the editor presents a critical review of several studies dealing with the prophylaxis of unipolar illness with lithium. It is posited that the utility of lithium in the prophylaxis of unipolar manic-depressive illness is strongly suggested but not proven by prospective random assignment placebo controlled studies. Although there is evidence from mirror image studies, it is recommended that these data should not be used in the final decision about lithium's prophylactic effect in unipolar illness. 14 references.

002158 Ruiz Ogara, C. Editorial Scientia, Peligro 39, Barcelona, Spain /Trazadone./ Trazadone. *Rev. de Psiquiatria y Psicología Med. de Europa y América Lat.* (Barcelona). 12(5):323, 1976.

Recommendations are given for the clinical indications for trazadone, a derivative of trizolopyridine which has no accumulative effects and which concentrates on the thalamus. It is concluded that it is well tolerated, its antidepressive action is rapid, and it possesses no dopaminergic, anti-MAO or anticholinergic properties.

002159 Sachar, Edward J. no address *Hormones, behavior, and psychopathology: papers from a meeting*. *American Psychopathological Association Series*. New York, Raven, 1976. 308 p. \$24.

A collection of papers covers advances in techniques for hormonal assays, advances in research strategy, and recognition of the complexity of the relationships among the various hormones, behavior, psychological stress, environmental conditions, and cognitive states. The first section covers hormonal influences on brain and behavior. Papers of interest to the clinician include a review of hormonal alteration of imipramine response, a paper on psychological correlates of the menstrual cycle and oral contraceptive medication, and an account of psychological disturbances associated with endocrine disease and hormone therapy. Papers drawing mainly on animal work include a review of the effects of adrenocorticotrophic hormone and vasopressin on motivation, learning, and memory and a discussion of polypeptide-releasing factors that originate in the hypothalamus and their effect on a variety of brain structures, particularly the anterior pituitary. Two papers focus on the effects of sex hormones on behavior. In the second section, the papers are more technical and cover the effects of brain and behavior on endocrine function. A paper on neuroendocrine effects of psychotropic drugs and two papers on anorexia nervosa have clinical relevance. Psychopharmacologists contributed several papers relating to drug action and neurotransmitter substances, one of which reviews neuroendocrine regulation in affective disorders.

002160 Schou, Mogens. Aarhus University Institute of Psychiatry, DK-8240 Risskov, Denmark *Current status of lithium therapy in affective disorders*. *Arquivos de Neuro-Psiquiatria* (Sao Paulo). 34(1):68-80, 1976.

Present and proposed uses of lithium in the treatment of affective disorders are discussed. It has only two accepted therapeutic uses: the treatment of mania and use in recurrent endogenous affective disorders. Tentative use of lithium for other disorders is discussed. These include depression, schizophrenia, recurrent endogenous affective disorders of the polar and the monopolar type, recurrent schizoaffective dis-

order, pathological emotional instability in children and adolescents, pathological periodic aggressiveness, periodic alcoholism with depression, opiate addiction, obsessive-compulsive neurosis, acute anxiety and premenstrual dysphoria. 78 references.

002161 Serban, George; Kling, Arthur. New York University Medical Center, New York, NY 10016 *Animal models in human psychobiology*. New York, Plenum, 1976. 300 p. \$22.50.

The implications for man of animal models are explored to gain understanding of biological, cultural, and environmental determinants of behavior. An international group of ethnologists, psychologists, and social scientists presents research into the nature of human behavior as compared with that of other animals. Topics discussed include: response to social separation in rhesus monkeys, human personality development, phylogenetic and cultural adaptation in human behavior, unpredictability in the etiology of behavioral deviations, and theories relating to behavior modification, electrical and chemical communication in the brain, drug effects, and indole hallucinogens and schizophrenia.

002162 Sheppard, Charles; Ricca, Elizabeth; Fracchia, John; Merlis, Sidney. Demographic and Special Studies Laboratory, Long Island Research Institute, Central Islip, NY 11722 *Chemotherapeutic preference of native and foreign specialists: a move toward consensus*. *Comprehensive Psychiatry*. 17(5):617-622, 1976.

The chemotherapeutic preferences of a sample of native and foreign psychiatrists were established in an attempt to determine the rationale underlying treatment practices in psychiatry. The specialists were surveyed for their procedural approach to a patient described as in crisis, experiencing an acute paranoid schizophrenic episode. The results showed that a wide variety of treatment preferences were employed, ranging from no chemotherapy, through differing single drug treatments, to combinations of psychotropic medications. It is concluded that the choice of drugs for native respondents would be one that is effective in reducing thought disorder, then psychomotor hyperactivity, namely a sedative phenothiazine, while foreign respondents considered drugs that were effective in reducing thought disorder, then inappropriate affect. 15 references.

002163 Sheppard, Charles; Ricca, Elizabeth; Fracchia, John; Merlis, Sidney. Central Islip Psychiatric Center, Islip, NY *Chemotherapeutic choices of native and foreign psychiatrists' preferences for an acute psychotic episode*. *Psychological Reports*. 39(2):343-350, 1976.

To gain further understanding of psychiatrists' prescription preferences, samples of native and foreign psychiatrists specializing in chemotherapeutic treatment were presented with a standard case of a male experiencing an acute psychotic episode for whom they were asked to develop a treatment program. The degree of concordance in chemotherapeutic preferences is considered, and data have shown little consensus. Ratings of symptom severity or hierarchy symptom importance were found to be quite similar. The foreign psychiatrists considered schizoaffective and undifferentiated schizophrenia significantly more frequently than native psychiatrists. Neither a symptom hierarchy nor diagnostic approach accounted for the variance observed in these drug preferences. 13 references. (Author abstract)

002164 Shopsin, Baron; Friedman, Eitan; Gershon, Samuel. Neuropsychopharmacology Research Unit, Department of

Psychiatry, New York University Medical center, 550 First Ave., New York, NY 10016 *Parachlorophenylalanine reversal of tranylcypromine effects in depressed patients*. *Archives of General Psychiatry*. 33(7):811-819, 1976.

Five hospitalized bipolar and unipolar endogenously depressed patients who showed an antidepressant response to the monoamine oxidase (MAO) inhibitor, tranylcypromine sulfate, and who relapsed when relatively small doses of p-chlorophenylalanine (PCPA) were added for brief periods are described. Considered with findings that PCPA similarly reversed the antidepressant effects of the tricyclic drug, imipramine hydrochloride, implications are: 1) serotonergic mechanisms are likely involved in the antidepressant effects of both the tricyclic drugs and MAO inhibitors in man; and 2) this indolamine may also play a role in the endogenous clinical state of depression. 43 references. (Author abstract modified)

002165 Simard, Normand. Clinique Roy-Rousseau, Quebec 5, Quebec, Canada */Prodigious development of psychopharmacology./ Essor prodigieux de la psychopharmacologie*. *Vie Médicale au Canada Français (Quebec)*. 5(7-8):735-737, 1976.

The origin and development of psychopharmacology over the past 20 years, with discoveries of psychotropic and neuroleptic drugs for the treatment of mental illness, are described. The discovery of the antipsychotic effect of chlorpromazine is equal to the discovery of penicillin in medicine. The growing use of psychotropic drugs in the world, especially Canada, is documented. Professionals who prescribe these drugs are identified. The therapeutic advantages of psychiatry and psychotherapy should not be ignored. 6 references.

002166 Solomon, Kenneth. Department of Psychiatry, Albany Medical College, Albany, NY 12208 *Benzodiazepines and neurotic anxiety: critique*. *New York State Journal of Medicine*. 76(13):2156-2164, 1976.

The chemistry, basic pharmacology and pharmacokinetics, behavioral pharmacology and clinical research data of the 4 benzodiazepines currently marketed in the United States are reviewed and related to the use of benzodiazepines as a modality in the treatment of neuroses and the anxiety associated with them. The difficulties in evaluating clinical studies include the difficulty in measuring anxiety since objective and subjective findings do not correlate well with each other, except in an acute situation, such as fear, and objective measurements measure only one time, which hinders the evaluation of anxiety as a process. Also, while nondouble-blind studies add experimental bias, there is no assurance that the double-blind controls for many other variables that may contaminate a study. Benzodiazepines may be efficacious in the treatment of neurotic anxiety, but not so efficacious as to obviate the need for concomitant psychotherapy and/or sociotherapy. Recommendations are given concerning dosage and selection of drugs. Directions for future research are outlined. 141 references.

002167 Steinfels, Margaret; Dach, Leslie. no address *MBD, drug research and the schools: a conference on medical responsibility and community control/February 13-14, 1976*. *Hastings Center Report*. June(supplement):1-23, 1976.

A conference on Medical Responsibility and Community Control was held to discuss the problem of the use of psychotropic drugs on school children, and an edited transcript is presented. Stimulus for the conference was a 1972 controversy in Boston over a research project testing the effects of three psychotropic drugs on learning difficulties and

behavior disorders. Also discussed is the use of drugs with minimal brain dysfunction (MBD), the validity of MBD as a diagnostic category, and the propriety of labeling children with this term. Discussion participants, including representatives of medicine, law, philosophy, and education, discuss the Boston project; the relation of such projects to the community involved; the roles of the community, the researchers, the schools, and the federal government (which funded the project); ethical aspects of research and treatment; and conflict resolution. 1 reference.

002168 Straker, M. Brentwood Veterans Administration Hospital, Los Angeles, CA **Clinical psychiatry and psychopharmacology -- a review.** *Journal of the American Pharmaceutical Association.* 16(10):557-559, 567, 1976.

In a seminar on psychopharmacology held at the University of California, in Los Angeles in February 1976, the need for an interdisciplinary approach to mental health care, particularly the need for collaboration between clinical psychiatrists and psychopharmacologists was discussed. The various roles of health professionals were noted, and a listing is provided of general mental health goals and specific patient treatment goals. Biological, psychological and social theories of mental illness are considered, and psychiatric treatment of mental illness is discussed, with drug therapy indicated as an important method of treatment. The complexities of drug choice, actions, interactions and hazards and side-effects are outlined. It is concluded that the clinical psychopharmacologist is a necessary member of the mental health team, who is able to serve as reinforcer, provider, observer, educator and advisor to both the patient and the mental health professional. 11 references.

002169 Todd, Malcolm C. Long Beach, CA **Caution: drug substitution can be hazardous to patient health. Repeal of patient protection statutes has resulted in therapeutic failures.** *Journal of the Indiana State Medical Association.* 69(11):801-802, 1976.

The dangers inherent in new drug substitution laws, already enacted in 19 states, that permit pharmacists to substitute cheaper generics for brand name products are discussed. Examples are presented in which therapeutic failures are traced to generic substitutions in prescriptions. It is felt that the medical community must make a better effort to inform state and national legislators, the public and the press of bioavailability problems with drugs that are considered to be the same chemically. New laws permitting drug substitution tend to drive a wedge between physician and pharmacist by promoting interchange without physician knowledge or approval and compound the subject of malpractice. Efforts to defeat legislative substitution plans and to communicate the reasons for the opposition are called for.

002170 Treegoob, Mark; Walker, Kenneth P. Devereux Foundation, Devon, PA **The use of stimulant drugs in the treatment of hyperactivity.** *School Psychology Digest.* 5(4):5-9, 1976.

The use of stimulant drugs in the treatment of hyperactivity in school children is discussed. Organically based hyperkinesis seems to benefit from drug treatment with stimulants; however, the lack of controlled studies, the possibility of placebo effect, the difficulty of distinguishing hyperkinesis from other symptoms, and the possibility for misuse and toxic effects make questionable long-term administration. It is emphasized that the administration of stimulants to children must be preceded by an adequate workup followed by observation and suitable adjunct procedures to insure that drug treatment is not prescribed merely on the basis of observations of disruptive or

inattentive behavior. Drugs discussed include Dexedrine, Ritalin and Cylert. 25 references.

002171 Wallace, Meredith; Singer, George. Department of Psychology, La Trobe University, Bundoora, Victoria 3083, Australia **Schedule induced behavior: a review of its generality, determinants and pharmacological data.** *Pharmacology Biochemistry and Behavior.* 5(4):483-490, 1976.

Work on schedule induced behaviors, including behaviors occurring in conjunction with nonconsummatory schedule parameters is reviewed. The topics range from wheel running in the rat to game playing and maze solving in humans. Pharmacological variables, including the effects of peripheral administration and central administration of several compounds, are also discussed. It is concluded that there may be either quantitative or qualitative differences in drug effects when schedule induced drinking is compared with deprivation induced drinking. A general activation theory that adjunctive behavior is the result of an increase in the excitability of motor pathways which lead through the lateral hypothalamus may account for the data presented in this and earlier reviews but is too broad in concept to make specific predictions about the relationships between schedule induced, and schedule controlled, behavior. 66 references. (Author abstract modified)

002172 Wardaszko-Lskowska, Halina. Klinika Psychiatryczna, Akademia Medyczna, Warsaw, Poland **Psychological and deontologic problems in relation to prolonged neuroleptic drug action.** *Problematyka psychologiczno-deontologiczna na marginesie leczenia środkami neuroleptycznymi o przedłużonym działaniu.* *Psychofarmakoterapia Schizofrenii Lek o Przedłużonym Działaniu.* Wrocław, Polskie Tow. Psychiat. Odd. Wrocławski, 1976. 256 p. (p. 47-52).

In a paper presented at a symposium on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wrocław, Poland, in October 1973, psychological and deontological problems related to prolonged action of neuroleptic drugs are examined in the context of freedom of choice of the schizophrenic patient and the ambiguity of the concept of normalcy. Administration of prolonged action drugs and the convenience of thereby removing troublesome patients from therapeutic contact is viewed as a potentially sophisticated means of compulsion on the part of the therapist.

002173 Weil, Andrew T. Botanical Museum, Harvard University, Oxford Street, Cambridge, MA 02138 **3,4-methylenedioxymphetamine and its effects.** *The love drug.* *Journal of Psychedelic Drugs.* 8(4):335-337, 1976.

The dosage, onset of action, duration of action, physical effects and psychopharmacological effects of the psychedelic amphetamine derivative 3,4-Methylenedioxymphetamine (MDA) are presented. MDA is labeled by the drug subculture as the "love drug," since it potentiates relaxation and a sense of well-being, which in turn permits the user to drop many of the barriers that exist in interpersonal relationships. The drug is described as producing a desireless, contented feeling without causing sensory distortions, hallucinations, or illusions. It is suggested that the FDA's declaration of MDA as a Schedule I drug (high abuse potential) may be prohibiting the development of its therapeutic value.

002174 Weissman, Myrna M.; Slobetz, Frank; Prusoff, Brigitte; Mezritz, Marjorie; Howard, Pat. Department of Psychiatry, Yale University School of Medicine, New Haven, CT **Clinical depression among narcotic addicts maintained on methadone in the community.** *American Journal of Psychiatry.* 133(12):1434-1438, 1976.

In a study of 106 predominantly young, lower social class men participating in a methadone maintenance program, about 1/3 were found moderately to severely depressed as assessed on standard rating scales of depression. The depressive symptoms were associated with a decrease in social functioning, increase in stress in the past 6 months, and a history of alcohol abuse. Because the combination of depression and drug addiction creates a high risk for suicide, depressive symptoms require early detection and treatment. The need for more research on treatment approaches, particularly the use of psychotropic drugs is suggested. 22 references. (Author abstract)

002175 White, James H. Division of Child and Adolescent Psychiatry, University of Texas Medical Branch, Galveston TX 77550 **Practical use of psychotropic drugs in children.** Texas Medicine. 72(9):48-52, 1976.

The use of psychotropic drugs to treat behavior problems in childhood and adolescence is discussed. Specific recommendations for appropriate drugs and dosages in treating hyperactivity, enuresis, pavor nocturnus (night terrors), somnambulism, and insomnia are presented. The goals which should be taken into account before psychopharmacologic intervention is undertaken and general principles to be followed in the treatment of psychiatric disorders of childhood and adolescence are also discussed. 13 references.

002176 Williams, Robert L.; Karacan, Ismet. no address **Pharmacology of sleep.** New York, John Wiley, 1976. 608 p. \$26.00.

Current information relating to drug effects on human sleep is presented, as measured by EEG parameters, including research and reports from several disciplines. Coverage includes drug interactions, a review of the biochemistry of sleep, a survey of the psychological aspects of sleep pharmacology, an objective method of pretesting the efficacy of sleep medications and their aftereffects, an evaluation of the process by which new sedatives and hypnotics are brought to market, and a survey of Food and Drug Administration drug evaluations. (Author abstract modified)

002177 Winstead, D. K.; Blackwell, B.; Eilers, M. K.; Anderson, A. no address **Psychotropic drug use in five city hospitals.** Diseases of the Nervous System. 37(9):504-509, 1976.

The use of psychotropic drugs on the acute short stay psychiatric units of five hospitals within the same city was studied. The nature and extent of drug use in general was explored with particular regard to the two major diagnoses of schizophrenia and depression. The staff attitudes to psychotropic drug use were examined. An evaluation was made of the impact of various patterns of drug usage on the patient's duration of stay. Data on 50 consecutive discharges from the five hospitals suggest that there is consensus on many aspects of psychotropic drug use and conformity with national trends. Drug selection and dosage tend to be conservative, but the use of drugs is often nonspecific except in the treatment of schizophrenia. The smaller differences between hospitals and attitudes to drugs, methods of use, and outcome mainly reflect the different populations and purposes which these hospitals serve. 13 references.

002178 Wolman, Benjamin B. no address **The therapist's handbook: treatment methods of mental disorders.** New York, Van Nostrand Reinhold, 1976. 539 p. L14.70.

Systematic and detailed descriptions of the various methods of somatic, drug, and psychotherapeutic treatment of mental disorders are provided for the general practitioner, the psychologist, and the social worker. Psychiatric syndromes and illnesses ranging from neuroses to schizophrenia are also described. Principles of psychotherapy are reviewed, behavioral therapy is discussed, and analytical methods are covered. Group therapy, family therapy, and psychopharmacology are briefly considered. Alcohol and drug abuse are also covered.

002179 Wolstenholme, G. E. W.; Knight, Julie. no address **/Monoamine oxidase and its inhibition./** Ciba Foundation Symposium 39. New York, American Elsevier, 1976. 415 p. \$29.95.

Papers and a general discussion held at a symposium on monoamine oxidase and its inhibition are presented. The classification of monamine oxidases is debated among biochemists, pharmacologists and behavior scientists. Investigations into the role of the enzyme in migraine, schizophrenia and depression are described.

002180 Yanaura, Saizo; Yamatake, Yoshikazu; Ouchi, Toyomi. Department of Pharmacology, Hoishi College of Pharmacy, Shinagawa-ku, Tokyo 142, Japan **A new analgesic testing method using ultrasonic stimulation: I. Effects of narcotic and nonnarcotic analgesics.** Japanese Journal of Pharmacology (Kyoto). 26(3):301-308, 1976.

A quantitative method for measuring pain threshold by the use of ultrasonic stimulation in mice is discussed. Male mice were used for most experiments. The method has the advantage of precision, simplicity of technique, rapidity of measurement, and the fact that the stimulus is innocuous upon repeated application. The nature of the sensations induced by ultrasonic stimulus is somewhat like that felt with a prick type of pain. Pentazocine, aminopyrine, phenacetin, sodium salicylate, and other antipyretic analgesics were active in a wide range of doses indicating that this technique is sensitive to the narcotic antagonist and to the weak analgesics as well as to the narcotic analgesics such as morphine, codeine, and pethidine. It is concluded that the ultrasonic method is applicable in screening procedures when attempting to evaluate the analgesic potency of a wide variety of chemical agents. 29 references. (Author abstract modified)

002181 Zentner, Joseph L. Department of Political Science, University of Southwestern Louisiana, PO Box 4-3762 USL, Lafayette, LA 70504 **The recreational use of LSD-25 and drug prohibition.** Journal of Psychedelic Drugs. 8(4):299-305, 1976.

The use of lysergic acid diethylamide-25 (LSD-25) and the application of criminal law in an attempt to prohibit its recreational use are discussed. Among the topics presented are: 1) possible medical and experimental uses for the drug; 2) the tendency of the drug to produce tolerance and physical liability; 3) court decisions concerning the use of psychedelic drugs for religious purposes; and 4) the passage of federal legislation and state legislation regulating the manufacture, distribution, possession and use of LSD-25. It is suggested that, although LSD-25 should not be made available to everyone to use under any and all conditions, the use of psychedelic drugs should be recognized as being primarily a sociological and public health matter, rather than a proper subject for the criminal law. 27 references.

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